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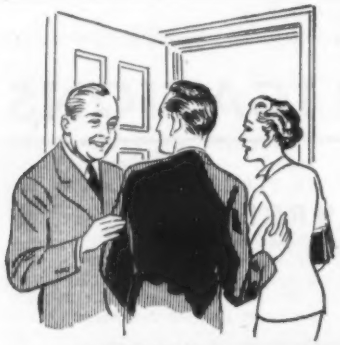

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Each tablet contains the *EFFECTIVE* oral penicillin, Penicillin-V Lilly, 125 mg. with a total of 0.5 Gm. of Sulphonamides (167 mg. each of) sulphadiazine, sulphamerazine and sulphadimidine. This combination is of particular value in mixed infections or where the organism is only moderately susceptible to either agent.

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Tablets 'PEN-V-SULPHA' are available in bottles of 20, 100, 500 and 1,000 scored tablets.

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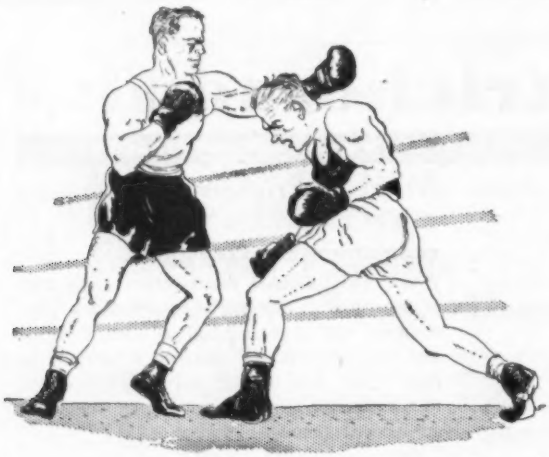

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ALGIPAN is available in 40 G. tubes.

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'Dettol' REGD. is active...

against both Gram-positive and Gram-negative micro-organisms.
Under standard conditions of test a dilution of 1 in 200 kills Staph. aureus in 10 minutes; a 1 in 500 dilution kills Strep. pyogenes in 10 minutes.

'Dettol'—retains a high degree of efficiency in the presence of organic matter.

'Dettol'—is not incompatible with soap, traces of which need not be removed before application.

'Dettol'—is non-poisonous and non-staining.

'Dettol'—is well tolerated by the skin and tissues.

INSTRUMENT 'DETTOL'
Instrument Dettol is widely used as a most effective and practical means of disinfecting surgical instruments—steel, stainless steel and plated, as well as glassware, rubber appliances and nylon sutures.

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Surgical Dettol is a specially formulated tincture for the surgical preparation of the skin. It remains actively bactericidal for a considerable period after drying. It dries quickly and leaves a non-slippery surface. Bactericidal action is not adversely affected by the use of ordinary soap solutions. Surgical Dettol in clinical use has proved non-toxic and non-irritant when used in accordance with the directions.

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CLINITEST and ACETEST

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Reagent Tablets
for the detection of Glycosuria

Reagent Tablets
for the detection of Ketonuria

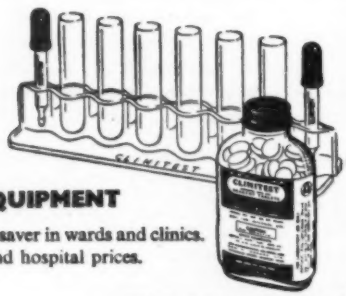
Both tests performed simultaneously in one minute!

Specialists, General Practitioners, Clinics and Hospitals in all parts of the country have used and prescribed 'Clinitest' Reagent Tablets since 1947. Many valuable hours have been saved. Now after intensive research work and clinical trials the makers of 'Clinitest' Reagent Tablets have produced 'Acetest' Reagent Tablets for the detection of Ketonuria. With 'Clinitest' and 'Acetest' Reagent Tablets, reliable routine sugar and acetone tests can be carried out *simultaneously* in one minute!

CLINITEST

No external heating · No measuring of reagents

Approved by the Medical Advisory Committee of the Diabetic Association. The 'Clinitest' set, refills and accessories are all available under the N.H.S. on Form E.C.10. (*Basic Drug Tariff Prices: Set 6/8 complete. Refill bottles of 36 tablets 2/4.*)



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The advantages of ACETEST Reagent Tablets

Quick and reliable, a single tablet provides all the reagents to perform a test. Low cost permits this tablet test to be used as a screening procedure or as a routine for diabetic patients. No danger of false positives with normal urine. No caustic reagents.

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Supplied in bottles of 100 tablets with colour scale.

'Acetest' Reagent Tablets (*diagnostic nitroprusside tabs.*) are also available under the N.H.S. on Form E.C.10. Basic Drug Tariff price 3/10 per bottle of 100 tablets (with colour scale).

REFERENCES

(1954) 'Clinical Tests for Ketonuria', '*Lancet*', *April 17th, pp. 801/804*
(1954) '*Medicine Illustrated*', *May, p. 289*
(1954) '*Practical Clinical Biochemistry*', *Heinemann, p. 74*
(1954) 'Clinical Tests for Ketonuria', '*Lancet*', *July 10th, p. 95*

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a waterproof, yet non-occlusive, adhesive first aid dressing that prevents maceration

Elastoplast 'Airstrip' is a new type of first aid dressing. It is made from a specially developed plastic material, through which sweat and skin exudates evaporate at the same rate as they develop on the skin. The material is, in fact, a micro-porous extensible filter, and is not perforated. It provides a barrier to water, grease, oil and infective organisms.

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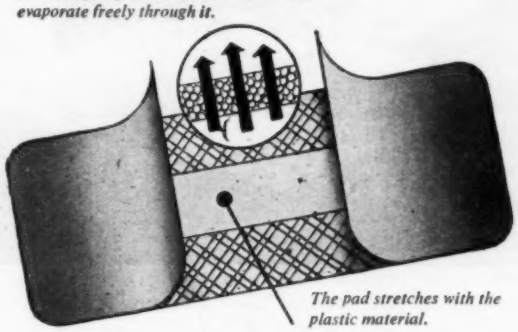

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100 dressings 1½"x ⅞" **9/8d.**
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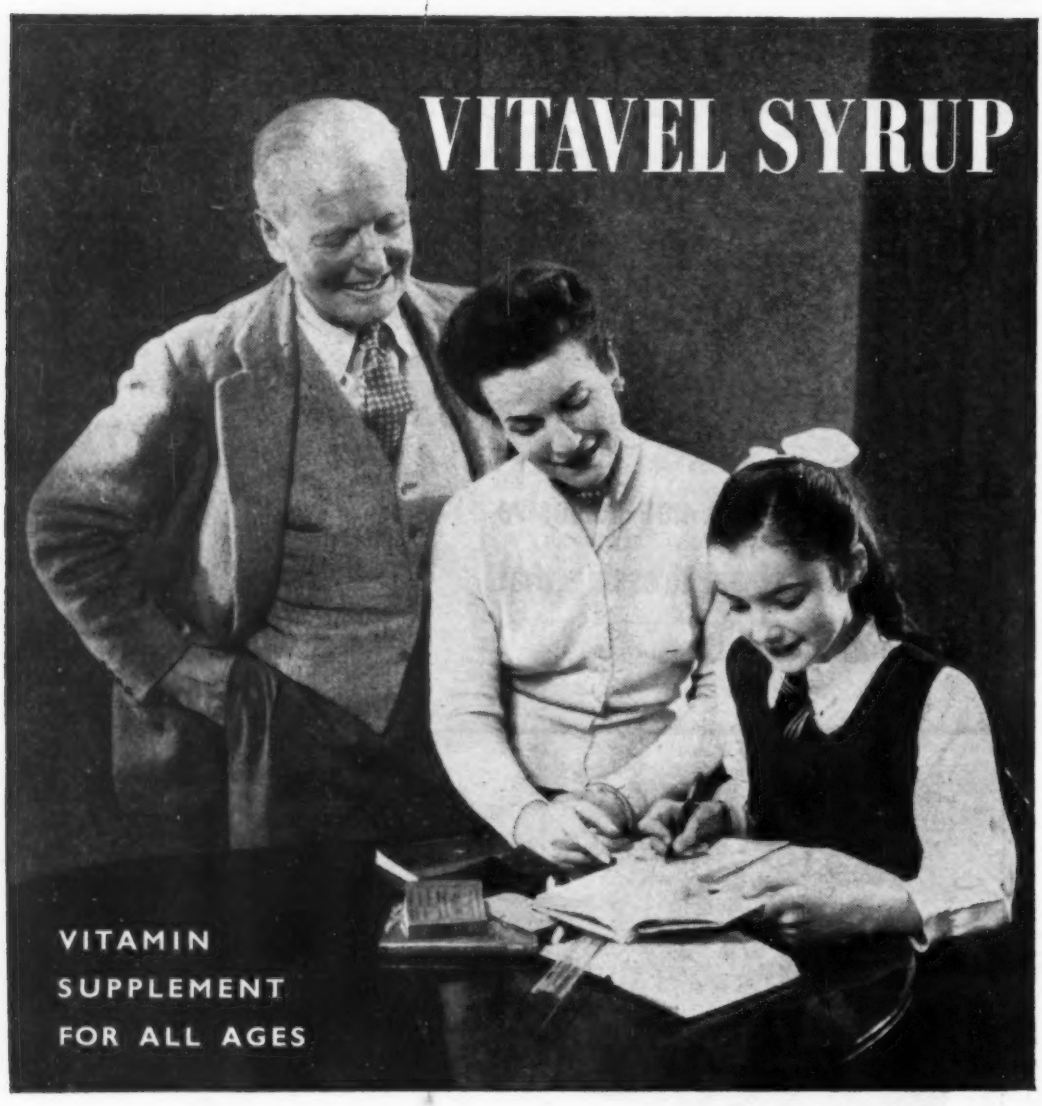
Less the usual professional discount.

PUBLIC PACK
sold by all chemists at **1/-** and **2/-** each.



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VITAMIN A 20,000 i.u. VITAMIN D 3,000 i.u. VITAMIN B_1 4 mg.
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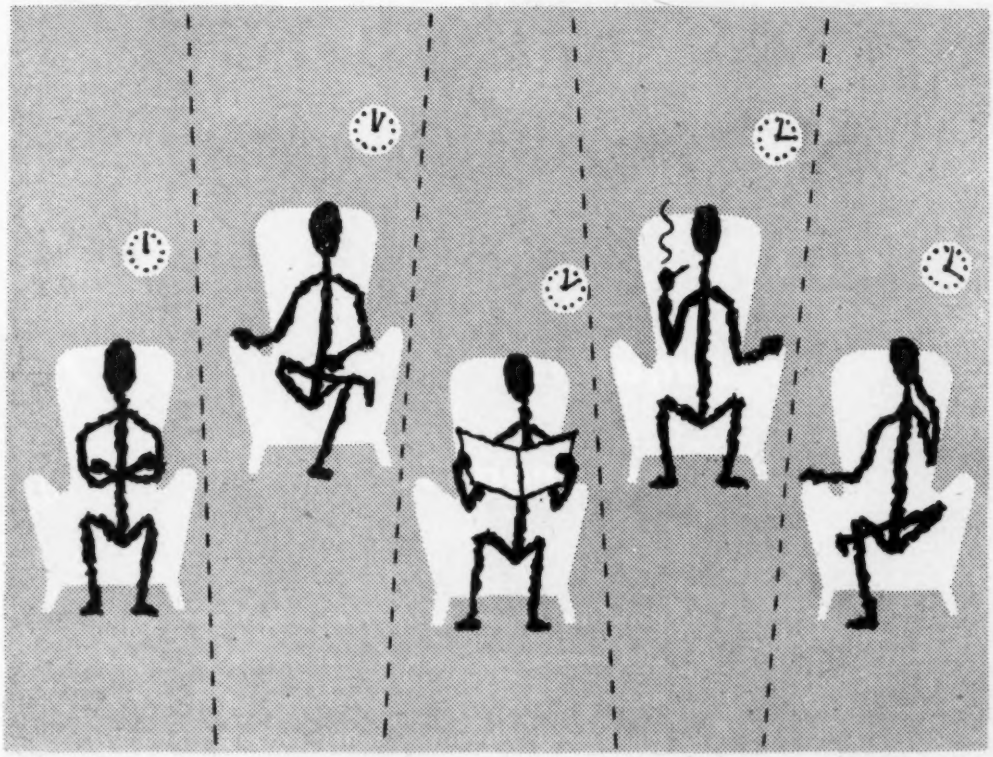

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The restlessness of many patients may well be traced to the torments of perineal pruritus, or haemorrhoids.

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Active Principles: Now embodied in colourless non-staining ointment base.

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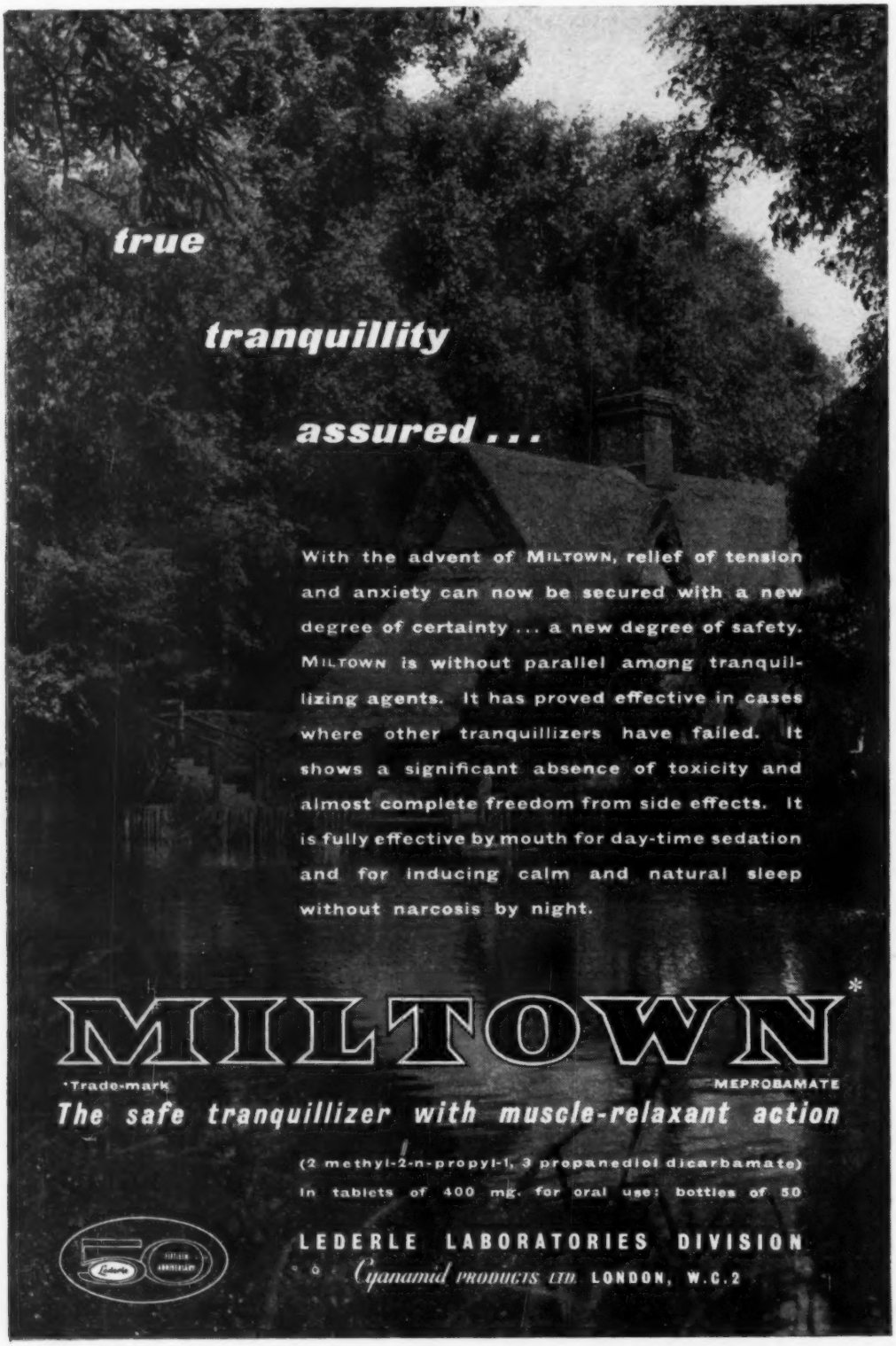
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Nulacin tablets are not advertised to the public, have no B.P. equivalent, and may be prescribed on E.C.10. The dispensing pack of 25 tablets is free of Purchase Tax. (Price to Pharmacists is 2/-.) Also available in tubes of 12.

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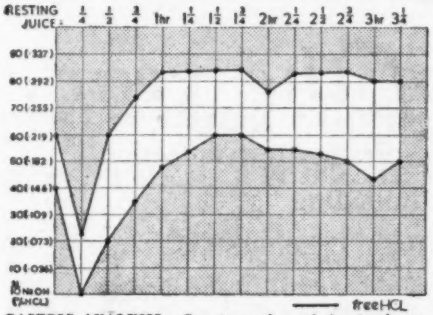
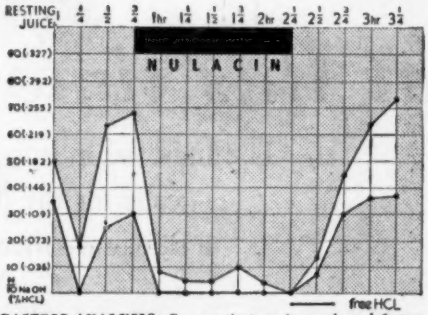


GASTRIC ANALYSIS. *Superimposed gruel fractional test-meal curves of five cases of duodenal ulcer.*



GASTRIC ANALYSIS. *Same patients as in graph on left, two days later, showing the striking neutralizing effect of sucking Nulacin tablets (3 an hour). Note the return of acidity when Nulacin is discontinued.*

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The Control of Gastric Acidity. *Brit. Med. J.* 26th July, 1952, **2**: 180-182. Medical Treatment of Peptic Ulcer. *Med Press* 27th February, 1952, **227**: 195-199. Notes on Remedial Agents. *Med Rev.* September, 1952, **46**: 162. Discussion on Peptic Ulceration. *Proc. Roy. Soc. Med.* May 1953, **46**: 354. The Effect on Gastric Acidity of "Nulacin" tablets. *Med. J. Aust.* 28th November, 1953, **2**: 823-824. Control of Gastric Acidity by a New Way of Antacid Administration. *J. Lab. Clin. Med.* 1953. **42**: 955. Further Studies on the Reduction of Gastric Acidity. *Brit. Med. J.* 23rd January, 1954, **1**: 183-184. Clinical Investigation into the Action of Antacids. *The Practitioner* July, 1954, **173**: 46. Management of Peptic Ulceration in General Practice. *Med. World* December, 1954, **81**: 591-601. Ambulatory continuous Drip Method in the Treatment of Peptic Ulcer. *Amer. J. Dig. Dis.* March, 1955, **22**: 67-71. Notes on Remedial Agents. *Med. Rev.* October, 1955, **49**: 142. Antacids in Peptic Ulcer. *The Practitioner*, January, 1956, **176**: 103.

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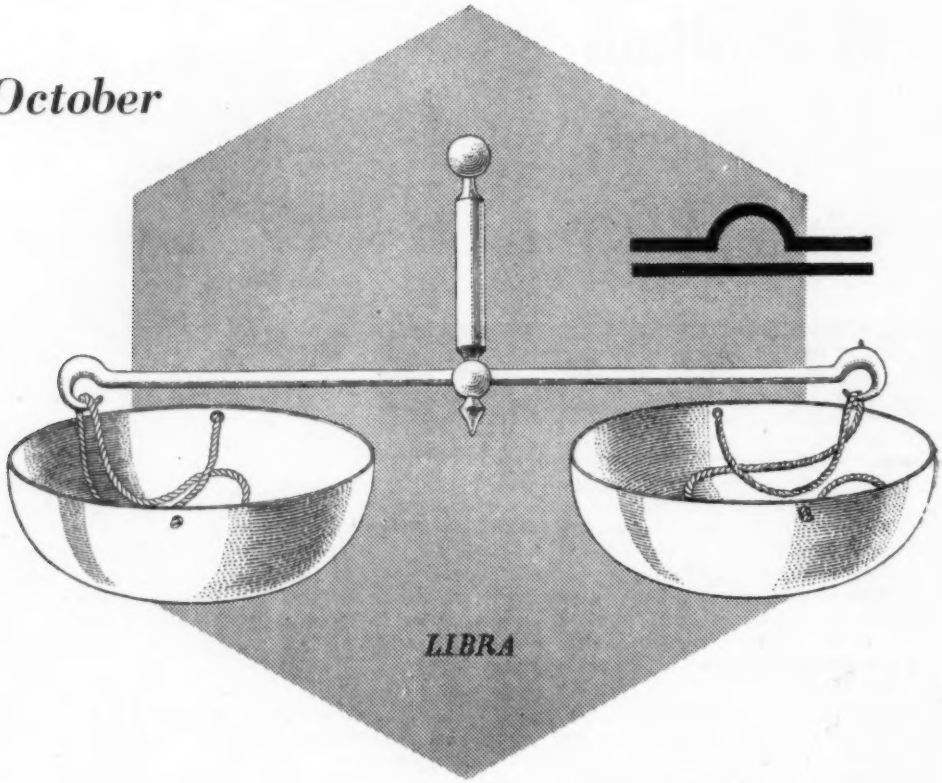

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* *Aerztl. Wochenschr.*, 34/35 : 788, 1955.

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When prescribing, most doctors prefer short words. So to save your time, and because so much 'Sulphamezathine' is prescribed, we have registered the abbreviation 'S-MEZ'. You can now use this shortened version officially, knowing that 'Sulphamezathine' will be dispensed. 'Sulphamezathine'—or 'S-MEZ'; they both stand for sulphadimidine. But 'S-MEZ' is quicker to write, and actually cheaper to prescribe, than sulphadimidine.

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19

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60 mg. scored tablets
Bottles of 30, 200 and 1,000

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ADULTS—One or more tablets at four-hourly intervals.
CHILDREN—Half the adult dose.

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30 mg. dose (1.75 ml.) Bottle of 2 fl. oz. (30 doses). A plastic spoon of 1.75 ml. (½ fl. dr.) is provided.

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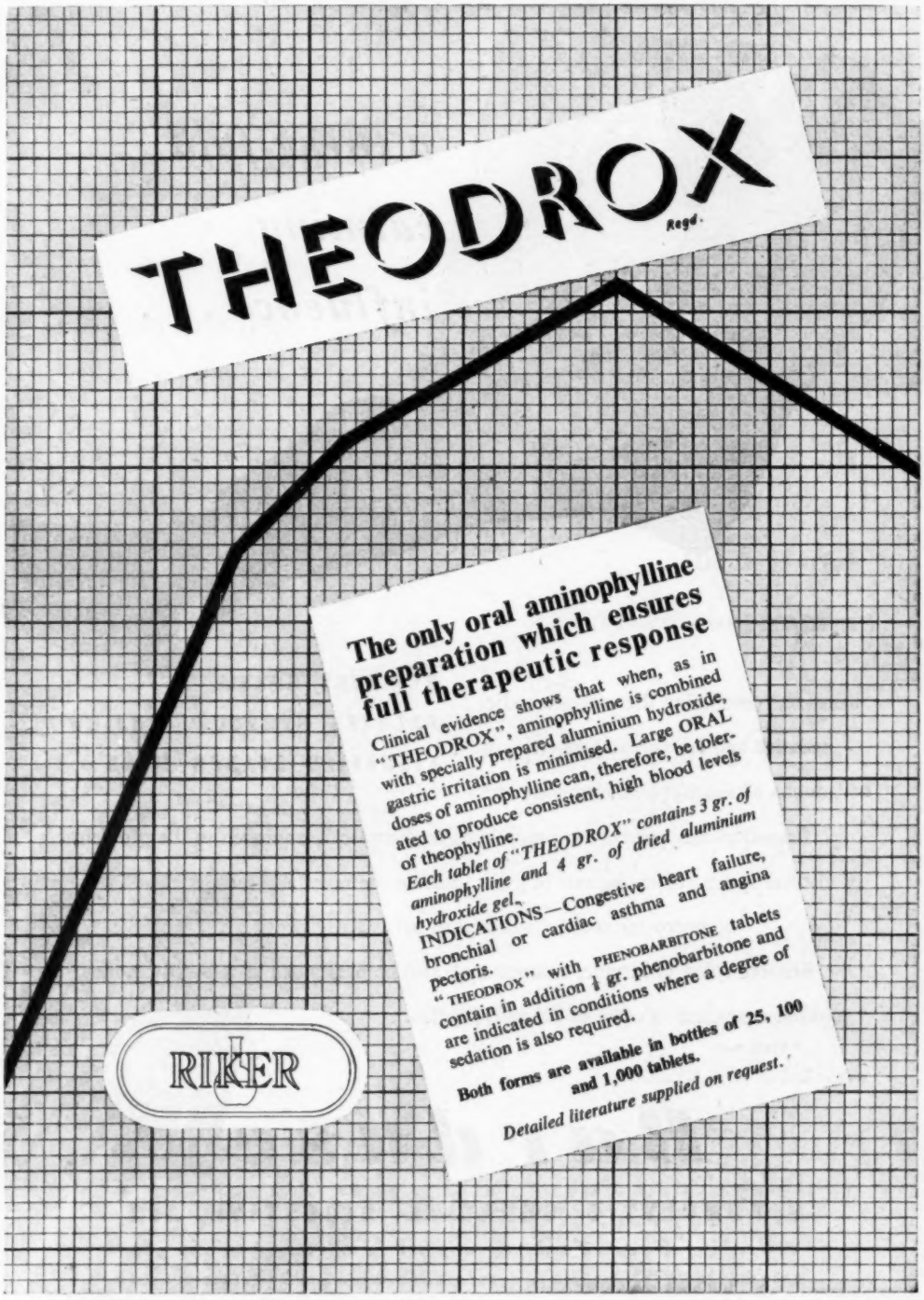
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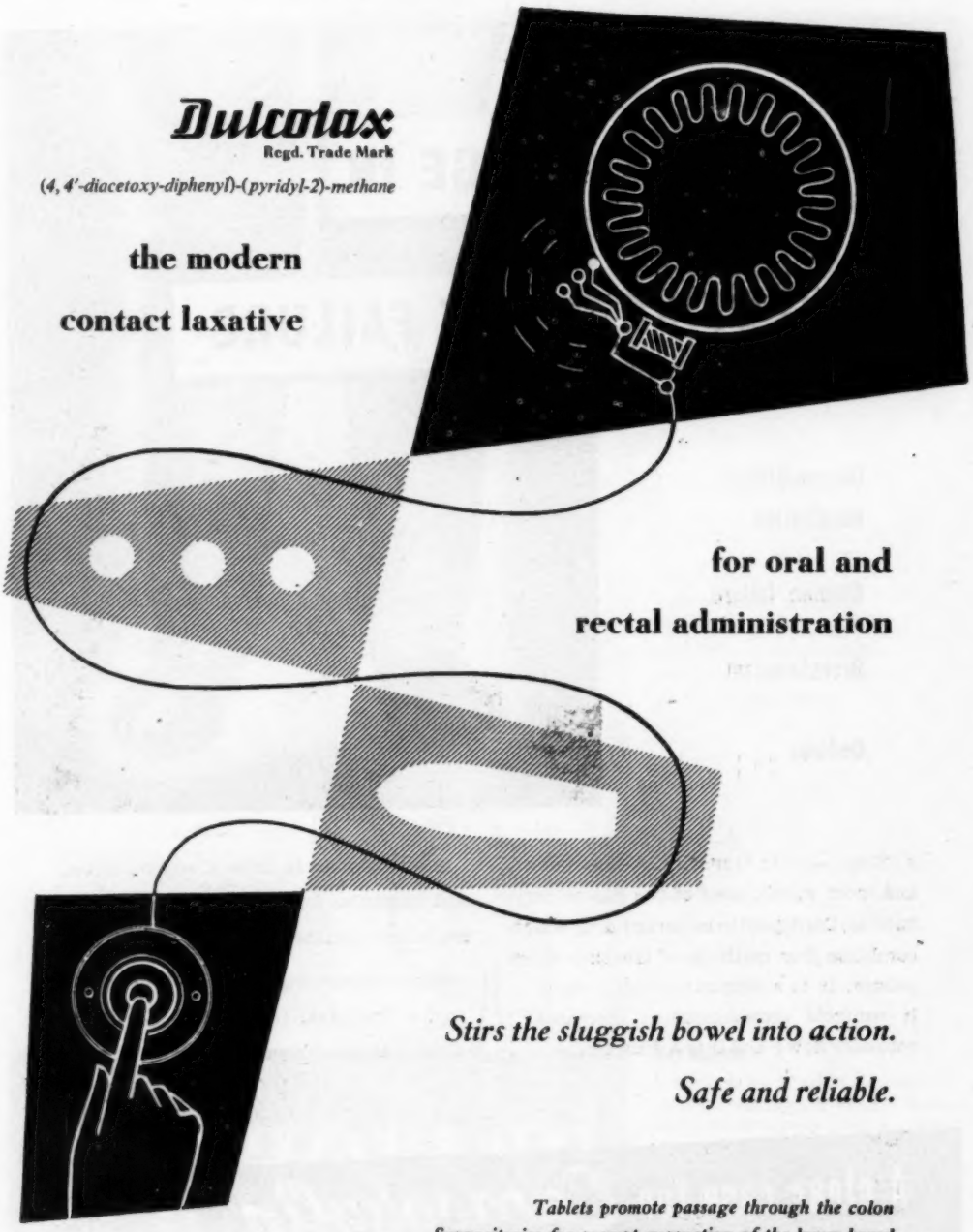

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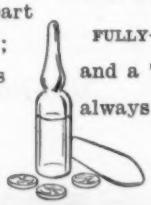

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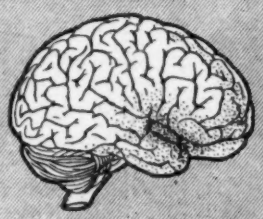
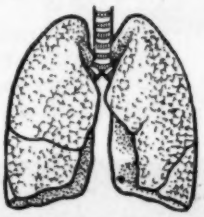
with only $\frac{1}{10}$ the central nervous system effect of ephedrine, Orthoxine avoids wakefulness and excitation, permits the asthmatic patient to **rest and relax.**





with twice the broncho-dilating effect of ephedrine, Orthoxine eases laboured respiration, provides more air for the asthmatic.

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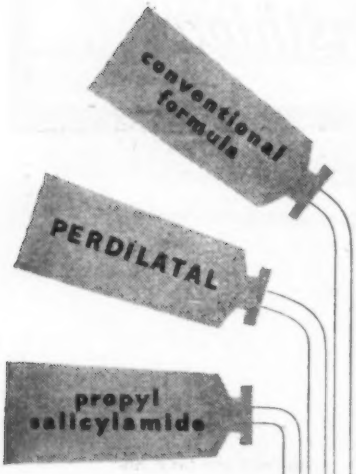

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PERDILATAL (formerly known as Dilatal), a powerful vasodilator which (when given systemically) increases muscle blood flow (1), and also produces a slight increase in cutaneous flow.

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Propyl salicylamide	5.0%
Methyl nicotinate	1.0%
Glycol salicylate	10.0%
Vanishing cream base	83.7%

(1) *Lancet*, 1956, *i*, 257.

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(1) The group of conditions covered by the terms 'muscular rheumatism' and 'fibrositis'.

(2) Local circulatory disorders where they have surface manifestations (e.g., chilblains, Raynaud's disease)

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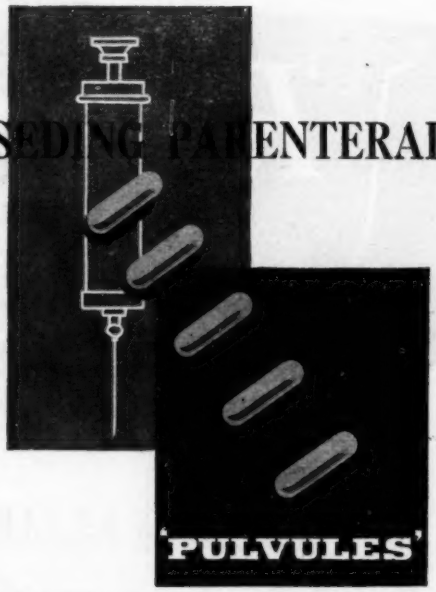

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THE TREATMENT AND PROGNOSIS OF HEPATIC COMA

SHEILA SHERLOCK
M.D. Edin., F.R.C.P.
PHYSICIAN AND LECTURER IN MEDICINE

W. H. J. SUMMERSKILL
M.A., D.M. Oxfd, M.R.C.P.
MEDICAL REGISTRAR AND TUTOR

A. M. DAWSON
M.B. Lond., M.R.C.P.
MEDICAL REGISTRAR

DEPARTMENT OF MEDICINE,
POSTGRADUATE MEDICAL SCHOOL OF LONDON

MENTAL symptoms and coma have long been regarded as very serious and often terminal complications of liver disease. Latterly, the mechanisms of their production have been better understood, and this has led to a more rational régime of treatment offering considerable hope of success. The newer knowledge of ætiology and course also allows results to be more accurately assessed. This paper describes the management of 66 patients in hepatic coma or pre-coma treated during the past three years.

A clinical picture similar to that of spontaneously developing hepatic coma can be induced in patients with liver disease by the oral administration of either a high-protein diet or nitrogenous substances such as ammonium salts, urea, and methionine (Phillips, Schwartz, Gabuzda, and Davidson 1952, Sherlock, Summerskill, White, and Phear 1954). The toxic, nitrogenous material in the intestines is believed to reach the systemic circulation, and thus the brain, by passing through a diseased liver, or through portal collateral vessels, or by both routes (portal-systemic encephalopathy) (Kirk 1936, White, Phear, Summerskill, and Sherlock 1955). This suggests that protein and nitrogen-containing drugs should be withdrawn from patients in impending hepatic coma. More recent investigation has shown that chlortetracycline, given by mouth, protects patients with liver disease from the adverse neurological effects of oral *dl*-methionine (Phear, Ruebner, Sherlock, and Summerskill 1956). The small-gut bacterial flora is increased in patients with hepatic cirrhosis, and the number of organisms and their effect on methionine is much reduced by the antibiotic (Martini, Phear, Ruebner, and Sherlock 1956). These findings support the recommendation of wide-spectrum antibiotic therapy by mouth. Finally gastro-intestinal hæmorrhage and any factor depressing liver function are common precipitants of hepatic coma, and the search for and control of these assume vital importance.

Patients Studied

66 consecutive patients (41 females and 25 males) with liver disease complicated by hepatic coma or pre-coma were treated. Diagnosis was based on clinical findings and serial biochemical tests, and was confirmed in 18 by aspiration liver biopsy and in 27 others at necropsy. Acute virus hepatitis (13 patients) was of either the serum or the infective type (table I). Hepatic cirrhosis (47 patients) was the most frequent underlying liver disease. These patients have been divided into an acute group with hepatic cirrhosis including biliary cirrhosis and acute neuropsychiatric episodes (table II) and a chronic group with well-compensated cirrhosis and a very large portal-systemic collateral circulation (table III). The latter had had neuropsychiatric symptoms and signs for many months before treatment (Summerskill, Davidson, Sherlock, and Steiner 1956). The miscellaneous group comprised 2 patients with obstructive jaundice and carcinoma involving the liver, 1 patient with renal carcinoma and Chiari's syndrome, 1 patient with ischæmic liver necrosis, and 2 patients with a normal needle biopsy of the liver and a large, natural portal-systemic circulation through a dilated inferior mesenteric vein (table IV).

Methods

The neuropsychiatric syndrome consists of progressive impairment of emotional control and intellect, the patient passing from stupor into coma. Common motor-system signs are a "flapping tremor" of the outstretched hands and increased muscle tone with hyper-reflexia and ankle-clonus. The neurological status was graded:

1. Minor disorders of consciousness and the motor system.
2. Gross disorder of consciousness with disorientation in time and space.
3. Coma.

The detailed symptomatology has been described elsewhere (Walshe 1951, Adams and Foley 1953, Sherlock et al. 1954, Summerskill et al. 1956). Grade 3, when the patient is unrousable, corresponds to the hepatic coma of older publications, for the importance of the pre-comatose states (grades 1 and 2) has been recognised only recently. The initial grade has been recorded and also the maximum grade reached after therapy. The syndrome is typically fluctuant and a second attack is so common that recovery has been defined as ability to be discharged home. Death from hepatic coma during the same hospital admission is counted as a therapeutic failure even though the patient may have survived one or more episodes. Numbers refer to patients and not attacks of coma. Death on a subsequent admission has been noted.

TABLE I—PATIENTS STUDIED: ACUTE VIRUS HEPATITIS

No.	Age and sex	Serum-bilirubin (mg. per 100 ml.)	Coma grade		Duration (days)		Result
			Initial	Maximum	Untreated	Of treatment	
1	56 F	20	1	1	1	3	R
2	29 F	39·4	1	1	5	3	R
3	4 F	5·2	1	1	4	21	R
4	22 M	21	2	3	4	4	R
5	10 F	13	3	3	4	3	R
6	64 M	26	3	3	8	5	D
7	52 F	14·4	3	3	3	45	D
8	25 F	29	3	3	14	1	D
9	32 F	22	3	3	5	15	D
10	30 F	18	3	3	1	7	D
11	59 M	20	1	1	1	3	R
12	48 M	23	3	3	2	3	D
13	56 M	3·6	2	2	6	5	R

D = died, R = recovered } in this and subsequent tables.

Ammonium levels in the peripheral venous blood were estimated using a minor modification of the Conway (1950) microdiffusion technique (Phear, Sherlock, and Summerskill 1955). Results are expressed as ammonium nitrogen μg. per ml.

Nitrogen balances were carried out in a metabolic ward. The patients were placed on a fixed nitrogen intake and three days were allowed for equilibration. The urine and fæces were then collected in two separate three-day pools. The fæces and a duplicated diet were homogenised and dried, and these, with the urine, were estimated for nitrogen by a modified micro-kjeldahl method. The nitrogen content of dietary rejects was estimated and was always less than 0·5 g. nitrogen per twenty-four hours.

Treatment

Three lines of treatment were used. The intestines were emptied and kept free of all nitrogen-containing

TABLE II—PATIENTS STUDIED: HEPATIC CIRRHOSIS (ACUTE TYPE)

No.	Age and sex	Ascites	Serum per 100 ml.		Precipitant	Coma grade		Duration (days)		Result	—
			Bilirubin (mg.)	Albumin (g.)		Initial	Maximum	Untreated	Of treatment		
14	50 M	+	3·2	2·1	Nil	2	3	1	5	D	Terminal melæna. Alcoholic
15	25 F	+	8·8	1·8	,,	3	3	2	9	D	
16	50 M	+	1·7	2·0	,,	1	3	1	8	D	Terminal melæna. Alcoholic
17	25 F	+	4·6	2·4	,,	2	3	1	8	R	Died 18 mos. later in coma
18	75 F	+	2·2	2·2	,,	3	3	6	49	D	
19	63 F	+	0·4	4·6	,,	1	3	1	3	D	
20	58 F	+	1·8	2·4	,,	1	2	1	28	R	
21	69 F	−	0·6	2·0	,,	3	3	2	3	R	
22	59 M	−	0·3	3·9	,,	1	1	1	4	R	
23	*61 M	−	2·6	3·6	,,	1	2	1	4	R	Died 6 mos. later in coma
24	57 M	+	19·6	2·1	,,	2	3	8	10	D	Terminal gastro-intestinal bleed Alcoholic
25	57 M	+	1·9	1·4	,,	2	3	5	6	D	Terminal melæna
26	72 M	+	0·7	3·2	Portal-vein thrombosis	1	3	1	5	D	Alcoholic. Also hepatoma
27	62 M	+	2·0	1·7	Paracentesis	1	3	1	8	D	Terminal melæna
28	50 F	+	1·3	2·8	G.I. hæm.	2	3	1	5	R	
29	36 F	−	2·1	3·2	G.I. hæm.	3	3	1	3	R	
30	56 F	−	1·8	3·4	G.I. hæm.	2	3	1	4	R	
31	59 M	+	2·5	3·1	Paracentesis	1	3	1	6	D	Also hepatoma. Alcoholic
32	52 F	+	16·0	2·3	G.I. hæm.	3	3	4	1	D	Alcoholic
33	72 M	+	4·0	2·4	G.I. hæm.	3	3	1	3	D	Alcoholic
34	56 F	+	2·9	2·2	Operative sepsis	3	3	16	3	D	Fractured femur
35	65 M	+	1·2	2·5	Pneumonia	2	3	4	8	D	
36	22 F	+	2·2	2·1	Operation	3	3	3	6	R	
37	30 M	−	..	..	G.I. hæm.	3	3	3	6	D	Thrombosed portal vein. Multiple hepatomata
38	*60 M	−	1·4	4·3	G.I. hæm.	2	3	3	3	R	Died 2 mos. later in coma
39	28 F	−	1·2	4·5	Operation	2	3	1	3	R	Died later exsanguinating hæmorrhage
40	51 M	+	1·2	3·2	Operation. Morphine G.I. hæm.	3	3	2	6 hr.	D	Terminal G.I. hæm. not controlled by Sengstaken tube. No autopsy
41	66 F	+	0·5	3·1	Operation	1	1	1	2	R	Alive 14 mos. later
42	18 M	+	2·5	2·1	Ammonium chloride	1	1	1	1	R	Alive 3½ years later
43	47 F	+	0·5	2·5	Paracentesis Ammonium chloride	1	2	1	4	R	Died 1 year later at home
44	*65 F	−	7·5	2·7	Operation	3	3	1	1	D	
45	*61 M	−	6·9	3·3	Operation. Sepsis	3	3	1	12	R	Alive 16 mos. later
46	56 F	+	2·1	2·8	Ammonium chloride	1	1	1	2	R	Alive 4 mos. later
47	52 M	+	1·7	3·1	G.I. hæm.	2	2	6	2	R	Alive 3 mos. later

G.I. hæm. = gastro-intestinal hæmorrhage. * Biliary cirrhosis.

material; chlortetracycline was given; and any precipitating factor was energetically treated.

Diet.—All dietary protein was stopped. At least 1600 calories were supplied daily as glucose drinks or as 20% glucose through an intragastric drip. When necessary, 40% dextrose was given intravenously through 'Polythene' tubing introduced via an antecubital vein into the innominate vein or superior vena cava. Small veins would be thrombosed by glucose of this strength. Care was taken to avoid fluid overload; urinary volume was measured and the lung bases and jugular-vein filling were examined regularly. Potassium supplements were often needed when glucose was the only source of calories. The exact amount was dictated by the history of the patient, the serum-potassium levels, and electrocardiographic changes.

Terminally there was often a fall in the serum-sodium level, a rise in blood-urea values, oliguria, and a fall in blood-pressure. Unsuccessful attempts to correct these changes with hypertonic sodium chloride were made on four occasions (Hecker and Sherlock 1956).

During recovery, protein was added in 20 g. increments on alternate days. The protein was divided between four meals. Any relapse was treated by a return to the former régime. Patients with an acute episode of coma soon achieved a normal dietary protein intake. In the chronic group, permanent protein restriction was needed to control mental symptoms (Summerskill et al. 1956); the limit of tolerance was usually 40–50 g. protein per day. In this group an exacerbation of symptoms was treated by rest, abstention from protein, and a short course of chlortetracycline.

TABLE III—PATIENTS STUDIED: HEPATIC CIRRHOSIS (CHRONIC NEUROPSYCHIATRIC DISTURBANCE)

No.	Age and sex	Principal collateral circulation	Ascites	Serum per 100 ml.		Maximum grade coma	Duration (months)		Remarks
				Bilirubin (mg.)	Albumin (g.)		Untreated	Of treatment	
48	43 M	Portocaval anastomosis	−	1·4	3·0	3	24	24	Died staphylococcal septicæmia
49	55 M	,, ,,	−	0·6	3·3	3	1	15	
50	42 M	,, ,,	−	0·9	2·8	3	6	9	
51	63 F	,, ,,	−	0·9	3·1	2	6	9	
52	50 F	Inferior mesenteric*	−	2·0	3·0	3	18	9	
53	52 F	,, ,,*	−	2·3	3·7	3	12	10	Died acute portal-vein thrombosis
54	41 F	Umbilical vein*	−	1·9	2·7	3	36	5	Died liver failure
55	39 M	,, ,,*	−	0·7	3·2	3	60	20	
56	59 M	Extensive œsophageal varices*	−	2·0	2·8	3	24	24	Died liver failure precipitated by congestive heart-failure
57	51 F	,, ,, ,,*	+	1·0	2·8	2	6	9	
58	36 M	,, ,, ,,*	+	1·1	2·4	3	72	2	Died acute portal-vein thrombosis
59	58 F	,, ,, ,,*	−	1·1	3·7	2	1	6	
60	57 F	Extensive œsophageal varices*	−	1·4	3·1	3	36	16	Died cerebral hæmorrhage

* Assessed by transplenic portal venography (Atkinson et al. 1955).

TABLE IV—PATIENTS STUDIED: MISCELLANEOUS GROUP

No.	Age and sex	Diagnosis	Coma grade		Duration (days)		Result
			Initial	Maximum	Untreated	Of treatment	
61	49 F	Primary extrahepatic portal-vein occlusion. Operation ..	1	1	1	3	R
62	76 F	Primary extrahepatic portal-vein occlusion. High-protein diet..	2	2	4	3	R
63	62 M	Chiari's syndrome. Hypernephroma	2	3	2	5	D
64	53 F	Secondary hepatic cancer. Obstructive jaundice..	2	3	3	8	D
65	65 F	Bile-duct cancer. Suppurative cholangitis	2	3	4	3	D
66	52 M	Low-output cardiac failure. Hepatic necrosis	1	3	2	4	D

Vitamins and Antibiotics.—Vitamin K and B complex supplements were given parenterally. The lower intestine was emptied by an enema, and this was repeated if necessary. Oral magnesium sulphate (*N.F*) 15 ml. daily was given, for some patients in the chronic group reported that they felt better when bowel actions were regular.

Oral chlortetracycline was given, if necessary, by stomach-tube, a loading dose of 2 g. being followed by 0·5 g. six-hourly for the duration of symptoms or to a maximum of one week.

Precipitating Factors.—Patients in impending coma were extremely sensitive to sedatives, all the symptoms and signs being exaggerated, and, where possible, these were avoided. If the patient was uncontrollable, half the usual dose of pentobarbitone was given; morphine was absolutely contra-indicated. Drugs known to induce hepatic coma—such as ammonium salts, ammonium exchange resins, methionine, urea, and acetazolamide ('Diamox')—were disallowed.

A common precipitant was gastro-intestinal hæmorrhage, usually from the œsophageal varices associated with portal hypertension. This increases the nitrogen content of the intestine, and the hypotension and anæmia further impair liver function. The bleeding may be a slow ooze, and overt hæmatemesis or melæna delayed for a few hours. Gastric contents should therefore be examined and a rectal examination performed in all patients where the

TABLE V—RESULTS OF TREATMENT OF PATIENTS WITH HEPATIC COMA

Disease	Total	No. reaching grade 3	Deaths
Acute virus hepatitis	13	8	6
Cirrhosis (acute group)	34	26	17
Cirrhosis (chronic group) ..	13	10	0
Miscellaneous	6	4	4
Total	66	48	27

precipitant of coma is uncertain. Gastro-intestinal hæmorrhage with hepatic coma was always an indication for the Sengstaken œsophageal compression balloon. Blood-transfusion was used to maintain the hæmoglobin level above 10 g. per 100 ml. This may need to be prolonged, and a piece of plastic tubing threaded into a large vein was often the surest way of delivering a constant supply of blood. Toxic products, including significant and increasing amounts of ammonium, develop rapidly in blood after shedding, and whenever possible fresh blood was used for transfusion.

Other factors impairing liver function included surgical trauma and anæsthetics, postoperative wound sepsis, and chest infections. These were treated along the usual lines.

Intravenous sodium glutamate in doses ranging from 23 to 72 g. was given on 12 occasions.

Results

Of the 66 patients treated, 48 reached deep coma. 39 (58%) recovered, 21 of the survivors having been in deep coma (grade 3) (table v). Of 34 patients with hepatic cirrhosis 17 survived, 9 following grade-3 coma; of 13 patients with acute virus hepatitis 6 survived, 2 following grade-3 coma. All the 13 patients in the chronic group with cirrhosis survived initial attacks of coma; 10 of these patients reached grade 3. Of the 6 patients in the miscellaneous group 2 recovered; neither had been deeply comatose.

TABLE VI—EFFECT OF INTRAVENOUS SODIUM GLUTAMATE IN HEPATIC COMA

No.	Intravenous sodium glutamate		Coma grade		Venous-blood ammonium nitrogen (µg. per ml.)		Result
	Amount (g.)	Duration (hours)	Before	After	Before	After	
12	40	30	3	3	2·1	..	D
14	23	24	2	2	1·2	2·1	D
38	72	24	2	2	2·5	3·6	D
42	23	3	1	1	2·59	1·96	R
44	23	8	3	3	1·5	..	D
60	46	10	2	2	2·9	1·1	R
	46	7	2	2	2·72	1·84	
	17	3	1	1	2·06	1·90	
63	46	48	2	2	2·2	0·98	D
64	23	24	2	2	1·67	0·65	D

Experience with Sodium Glutamate (table VI).—8 comatose patients, in whom protein withdrawal and chlortetracycline therapy had failed, received intravenous sodium glutamate in doses of 23–40 g. over twenty-four hours. None showed any improvement during or after the infusion and all died. The same doses were given on 4 occasions to 2 patients in impending coma and on a constant protein intake, without influencing the clinical condition. Peripheral-vein ammonium levels were determined before and after the infusion on 9 occasions with a reduction in 7 instances.

Effects of Dietary Protein Restriction (table VII).—Patients with acute episodes of coma recovered after complete protein withdrawal for many days. 7 patients

TABLE VII—RESULT OF PROLONGED PROTEIN RESTRICTION FOR THE TREATMENT OF CHRONIC PORTAL SYSTEMIC ENCEPHALOPATHY

No.	Dietary protein		Duration of protein restriction (months)	Weight (kg.)		Ascites		Ankle œdema		Serum-albumin (g. per 100 ml.)		Nitrogen balance (g. per 24 hr.)
	Total (g.)	g. per kg. body-weight		Before	After	Before	After	Before	After	Before	After	
48	40	0·58	20	75	70	0	0	+	+	3·0	2·9	+0·1
50	70	1·05	9	68	70	0	0	0	0	2·8	2·8	+3
52	50	0·7	9	71	6	0	0	0	0	3·0	3·3	+0·9
53	40	0·6	10	60	60	+	+	+	+	2·7	2·5	+0·8
54	20	0·58	5	37	37	0	0	0	+	2·7	2·7	+0·25
55	50	0·7	20	71	69	0	0	0	0	3·2	2·9	..
56	45	0·56	22	68	69	–	–	–	–	2·8	2·9	..
58	40	0·62	2	65	62	+	+	+	+	2·4	2·4	..
59	50	0·57	6	58	59	–	–	–	–	3·7	3·6	..
60	50	0·80	10	63	61	–	–	–	–	3·1	2·7	..

survived more than five days' protein abstention. Certainly in the acute group protein deprivation did not prevent ultimate recovery.

Signs of protein deprivation were not seen in the chronic group given low-protein diets for many months. In fact the 5 patients tested were in positive nitrogen balance on 20–70 g. protein daily (0·58–1·05 g. per kg. body-weight). 13 patients have received low-protein diets for periods ranging from two to twenty-four months. Body-weight has been maintained. Clinical ascites and œdema have not appeared (or, when present, have not increased): indeed, 1 patient lost her ascites. Serum-albumin levels have fluctuated without significant change.

FACTORS AFFECTING PROGNOSIS

(Tables v and viii)

Diagnosis.—Acute hepatitis was a more serious cause of coma than cirrhosis, particularly if deep coma developed (table v). The chronic group in whom raised dietary nitrogen is a major factor will usually recover if dietary protein is withdrawn. The prognosis in the miscellaneous group depends mainly on the underlying disease. Death may be expected in the cancer group, while the patients with extrahepatic portal-vein obstruction will recover if the additional insult depressing liver function can be controlled.

Age.—In the patients with virus hepatitis, age did not affect the outlook. The patients with cirrhosis seemed to withstand deep coma better if they were younger, although the number in the younger group was small.

Sex.—This did not affect prognosis in patients with virus hepatitis. The female patients with cirrhosis withstood deep coma better than the men, 6 of 12 women recovering from deep coma whereas only 2 of 12 men survived.

Duration of Symptoms before Treatment.—Prognosis was unaltered provided treatment was begun during the first week of symptoms. This is surprising, for it had been thought that early treatment would probably be successful. Many patients in deep coma, however, had been transferred from other hospitals and died rapidly. Those patients had almost certainly experienced unrecognised prodromata for much longer than the time stated on the case-charts. All 4 patients with symptoms lasting more than one week died.

Depth when Treatment Started.—17 patients were first seen in grade 1, and 12 of these recovered: the 5 patients who deteriorated while being treated all died. 18 patients were first seen in grade 3 and only 7 recovered. Treatment is therefore more likely to be successful if measures are initiated in the pre-comatose state. If there is no improvement in the first two or three days, ultimate recovery is unlikely, although 1 patient (no. 17) survived eight days of deep coma.

TABLE VIII—FACTORS AFFECTING PROGNOSIS IN ACUTE HEPATIC COMA COMPLICATING HEPATIC CIRRHOSIS

—		Patients all grades	Patients reaching grade-3 coma	Deaths
Total		34	26	17
Age (years)	>50	26	20	15
	<50	8	6	2
Sex	M	17	13	11
	F	17	13	6
Ascites	+	22	17	14
	−	12	9	3
Serum-bilirubin *† (mg. per 100 ml.)	> 3	6	6	5
	< 3	23	16	10
Serum albumin (g. per 100 ml.)	> 3	13	9	4
	< 3	20	16	12
Precipitating factor	+	22	17	10
	−	12	9	7
Grade when patient first seen	1	13	5	5
	2	9	9	4
	3	12	12	8

* Four patients with biliary cirrhosis are excluded.
† One patient died within a few hours of admission and serum-bilirubin and serum-albumin levels were not measured.

Hepato-cellular Function.—In acute hepatitis the serum-bilirubin level was used as an index of liver-cell function. The patients were deeply jaundiced, 8 of the 13 having serum-bilirubin levels greater than 20 mg. per 100 ml. 2 patients with serum-bilirubin levels less than 10 mg. were not deeply comatose; otherwise the depth of jaundice did not affect prognosis.

In hepatic cirrhosis, the presence of ascites, and the serum-bilirubin and serum-albumin levels, were used to evaluate hepato-cellular function.

Ascites was a most ominous association. 14 of the 16 patients with ascites who reached deep coma died, whereas there were only 3 deaths among the 9 grade-3 patients without ascites. The serum-bilirubin level was greater than 3 mg. per 100 ml. in 6 patients with portal or post-necrotic cirrhosis: all reached grade 3, and 5 died. 23 patients had serum-bilirubin values below 3 mg. per 100 ml. 15 of these reached grade 3 and 10 died. Jaundice is therefore also a bad prognostic sign. A low serum-albumin level also affected the prognosis adversely. 20 patients had a serum-albumin level less than 3 g. per 100 ml.: 15 reached grade 3 and 12 died. 13 patients showed a serum-albumin level greater than 3 g. per 100 ml.: 9 reached grade-3 coma but only 4 died.

Precipitating Factors.—In the acute hepatitis group, precipitating factors did not seem to affect the prognosis. Additional factors were obvious in 22 patients with cirrhosis: 16 were deeply comatose and 10 died. In 8 patients the precipitant was gastro-intestinal hæmorrhage, and in 7 patients the coma was postoperative: in each group 6 patients became deeply comatose and 3 died. Other factors were pneumonia (1 patient), paracentesis (3 patients), portal-vein thrombosis (1 patient), and high-protein diet with ammonium chloride supplements (2 patients). In 12 patients no precipitating factor was found: 9 became deeply comatose and 7 died. This supports the view that the prognosis is better if there is an easily controllable precipitating factor.

Gastro-intestinal hæmorrhage complicated already established hepatic coma in 5 patients and was always fatal.

Long-term Prognosis.—If a patient with acute hepatitis survives hepatic coma, recovery is usually complete. Only 1 patient has developed clinical post-hepatitis cirrhosis: the others are well two months to two years later.

7 of 8 patients with cirrhosis surviving grade-3 coma, and 5 of 9 surviving grade 1 or 2, are alive one year later. 2 patients recovering from grade-2 coma are alive six and two months later. Deaths have occurred two months, six months, and one year after discharge from hospital—from gastro-intestinal hæmorrhage or a further episode of coma.

Of 13 patients with chronic portal systemic encephalopathy, 7 are still alive and symptomatically relieved, 2 for longer than a year and 5 for longer than six months. 2 patients lived for twenty-four and twenty-two months and then died, one of liver failure precipitated by congestive heart-failure, and the other of a staphylococcal septicæmia. Only 2 patients died within six months of starting treatment (both of liver failure); 2 patients died after ten months (1 from a cerebral hæmorrhage and 1 from liver failure).

Discussion

The grave prognosis of hepatic coma is generally accepted, and is emphasised by the recent report of Foulk et al. (1955) who found only 5 recoveries in 52 patients treated at the Mayo Clinic. In coma due to virus hepatitis, Ducci and Katz (1952) saw no recoveries among 1000 consecutive patients, and Stokes et al. (1945) found only 2 survivors in 23 patients. McDermott and his group (1955) report only 4 survivors among 20 patients with acute coma, usually due to portal cirrhosis. The present results therefore stand comparison with those previously described; for 11 of 34 patients in deep coma due to virus hepatitis or cirrhosis survived. Results are even more impressive if the pre-comatose state is included; for 23 of the 47 patients survived. It is, of course, impossible to predict whether if untreated these patients would have passed from the pre-comatose state to deep coma, or how many would have recovered without treatment.

Assessment of therapeutic results in hepatic coma is complicated by the unpredictable fluctuations in its clinical course and the variable response to treatment of the numerous precipitating factors. Investigations should therefore be conducted on large series of patients on controlled régimes, with recovery (defined as ability to be discharged from hospital) as the sole criterion of success. Patients with chronic portal systemic encephalopathy (chronic intermittent hepatic stupor) must be separated from the acute group; for in these patients, provided oral protein is withheld, spontaneous recovery is the rule.

Treatment is based on the concept that a toxic nitrogenous substance formed in the intestine by bacterial action is at least in part responsible for the altered cerebral metabolism of hepatic coma. It has been suggested that the substance is ammonium, which could theoretically disturb cerebral metabolism (Bessman and Bessman 1955). Blood-ammonium levels are frequently, although not constantly, raised in patients with hepatic coma (Mann et al. 1954, Traeger et al. 1954, Phear et al. 1955). Speculation about the nature of the toxic substance does not affect the efficacy of withdrawing dietary protein. In the acute cases a few days' to a few weeks' deprivation of protein did not prove harmful; and even in the chronic group, in whom dietary protein had to be restricted for many months, clinical protein malnutrition was not seen. These findings support the observation that patients with liver disease can maintain nitrogenous equilibrium on a severely reduced intake of protein (Gabuzda and Davidson 1954), and the risk of temporary nitrogen depletion is preferable to the hazards of nitrogen toxicity. This measure, however, is indicated only in patients showing signs of coma. Other patients with liver disease may benefit from high-protein feeding, particularly if they are forming ascites (Patek et al. 1948). Glucose provides a ready source of energy, and Jones (1936) noted a 30% fall in the mortality of acute hepatic insufficiency when intensive glucose therapy was used.

Chlortetracycline prevents massive hepatic necrosis in rats fed on a necrogenic diet (Gyorgy et al. 1950)—an effect attributed to elimination of intestinal bacteria utilising protective constituents of food. It seems more likely, however, that the beneficial effect in our patients was due to changing the intestinal flora so that less toxic material was produced (Phear et al. 1956). Diarrhœa may complicate chlortetracycline therapy and necessitate withdrawal of the antibiotic. Long-term use is also associated with the emergence of resistant organisms and was not attempted. Fisher and Faloon (1956) have reported the continued use of neomycin in the group with chronic neuropsychiatric changes. Neomycin may well be the more satisfactory antibiotic for routine use in the treatment of hepatic coma, although at present its cost is prohibitive.

Glutamic-acid therapy is based on the supposition that ammonium toxicity is important in the genesis of hepatic coma. Glutamic acid should react with the ammonium, forming innocuous glutamine (Walshe 1953). Good results have been claimed in small series (Walshe 1953, Priest et al. 1953) although this has not been confirmed by wider application under controlled conditions (Sherlock et al. 1954, Alexander et al. 1955). Certainly, in the present patients clinical results were poor although blood-ammonium levels often fell. McDermott and co-workers (1955) have reported good results in the group with coma due to gastro-intestinal hæmorrhage or intolerance of nitrogenous substances. Results however, were no better than in comparable patients in the present series treated only with protein restriction and chlortetracycline. Failures were also reported by Webster and Davidson (1956), although these authors found that very large amounts of the substance (over 100 g. daily) seemed to be of temporary benefit in 2 and possibly 3 patients with cirrhosis. Results are not sufficiently convincing to recommend the routine use of sodium glutamate in hepatic coma.

The importance of the immediate treatment of any precipitating factor, together with the most careful nursing and medical attention, cannot be overstressed. Gastro-intestinal hæmorrhage was the commonest precipitant and should always be suspected in any patient with liver disease developing unexplained neurological changes. The Sengstaken œsophageal compression tube was a life-saving adjunct to treatment.

Minor surgical procedures were poorly tolerated, and where possible should be avoided in the presence of known liver damage. If they are inevitable, preoperative measures should include restriction of dietary protein and a course of chlortetracycline or neomycin. Increased dietary protein, or drugs such as ammonium chloride or acetazolamide, was of major importance only as a precipitant in the chronic group in whom coma is rarely fatal.

Hepatic coma has been divided into endogenous (patients with advanced liver disease without a clear precipitant), and exogenous (patients with reasonably well-compensated liver disease in whom precipitating factors can be incriminated) (McDermott et al. 1955). This is not a clear-cut classification, for neuropsychiatric features and electro-encephalographic records are identical and there is no diagnostic biochemical differentiation between the groups. A multiplicity of precipitating factors may occur in the same patient, and gastro-intestinal hæmorrhage—a frequent association of coma—impairs liver function as well as increasing nitrogen in the intestine. Hæmorrhage is also common in patients already comatose. It is not surprising, however, that the prognosis was better in the group with a clear precipitant; for this indicates a positive line of therapy.

Prognosis depends on the extent of liver-cell failure. The chronic group with relatively good liver function but with an extensive collateral circulation, combined with increased intestinal nitrogen, have the best prognosis, and the acute hepatitis group the worst. In cirrhosis the outlook is poor if the patient has ascites, jaundice, and a low serum-albumin level—all indicative of poor liver-cell function. If treatment is begun early in the pre-comatose state, the chances of success are increased.

The therapy of hepatic coma is only one facet of the whole management of the patient with chronic liver disease. The chances of the patient developing another complication or of coma recurring are considerable. The majority of survivors, however, were alive one year later, and treatment is eminently worth while. This is

particularly true of the acute hepatitis group, in whom recovery is usually complete. Altered liver function, allowing the passage of toxic nitrogenous substances from the intestine to the brain, is only one aspect of liver failure. The régime described cannot control the electrolyte disturbances and other unrecognised metabolic changes which must be occurring when the liver fails. Moreover no treatment directed solely towards correction of altered cerebral metabolism can be expected to constantly succeed in these circumstances. This conservative régime is suggested as the best available and will be modified when other effective remedies are discovered.

Summary

A régime of treatment for hepatic coma is described based on withdrawal of dietary protein and treatment with broad-spectrum antibiotics. Precipitating factors are energetically treated. The régime is based on the concept that toxic nitrogenous substances of intestinal origin can be incriminated in the pathogenesis of hepatic coma.

39 of 66 patients recovered, 21 of the survivors having been in acute deep coma.

Intravenous sodium glutamate was given on 12 occasions without clinical improvement.

13 patients with chronic neuropsychiatric changes (chronic portal-systemic encephalopathy) were maintained on low-protein diets for two to twenty-four months without showing signs of protein malnutrition, and serum-albumin levels were well maintained.

Prognosis was better in cirrhosis than in acute virus hepatitis, and if treatment was initiated in the precomatose stage. Outlook was also better when a clear precipitating factor, such as gastro-intestinal hæmorrhage, was amenable to therapy.

In cirrhotic patients, when coma was associated with signs of liver failure—such as ascites, jaundice, or a low serum-albumin value—the prognosis was bad. Survivors in the acute hepatitis group usually made a complete recovery. 7 of 8 patients with cirrhosis who survived deep coma were alive a year later.

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ANARTHRITIC RHEUMATOID DISEASE

L. BAGRATUNI
M.A., B.M. Oxfd

GRADUATE ASSISTANT, DEPARTMENT OF CLINICAL BIOCHEMISTRY, RADCLIFFE INFIRMARY, OXFORD

7 cases of a syndrome affecting the elderly and bearing a remarkable resemblance to the prodromal symptoms of rheumatoid arthritis before the joints are involved have already been published (Bagratuni 1953). It was then emphasised that rheumatoid arthritis need not run a typical course to frank arthritis, and that insistence on the involvement of joints may lead to the neglect of related conditions with a better prognosis.

I report here 17 further cases of the syndrome without involvement of the joints and 4 cases in which involvement of the joints was minimal. These last 4 cases form a link between the anarthritic form of the syndrome and true rheumatoid arthritis. Apart from swelling of the joints, the symptoms and signs in the two groups are identical.

The Syndrome

The syndrome occurs in middle-aged and elderly men and women and starts as a pyrexial illness with sweating, loss of appetite and weight, anæmia, and general malaise. Often there are abdominal discomfort (flatulence, vomiting, or diarrhœa) and headache. At the same time there is generalised aching which is confined to the muscles and is characteristically most severe in the neck, shoulders, and back. Rarely the pain may be in the chest and abdomen. There is stiffness of the muscles, and paræsthesiæ may develop in the limbs. The pain in the neck, shoulders, and back is so severe that active movement is often impossible, although there is no obvious arthritis. Passive movement is usually full, though painful. Rheumatic nodules and rashes may appear in the skin. Vomiting and diarrhœa, although not invariable, show the generalised nature of the disease process, which is also reflected in the pyrexia, tachycardia, anæmia, and loss of weight.

On examination there is usually remarkably little to find, apart from muscle pain, limitation of limb movement, occasional enlarged lymph-nodes, and rarely an enlarged spleen. Most cases present as pyrexia of unknown origin, especially if the aching succeeds the fever. A characteristic finding is a very high erythrocyte-sedimentation rate (E.S.R.), usually about 100 mm. in one hour (Westergren), and often well above this figure. The hæmoglobin is decreased because of secondary iron-resistant anæmia. The white-cell count is usually within normal limits, but there may be a slight leucocytosis or leucopenia, with or without abnormal white cells in the peripheral blood.

The albumin/globulin ratio in the plasma is altered, with a decrease in the albumin and an increase in the α_1, α_2, and sometimes γ globulin fractions. This change may be severe enough to reverse the albumin/globulin ratio. Cryoglobulins may be present, and the differential sheep-cell agglutination test is sometimes positive. The plasma-fibrinogen level is invariably high, often reaching a value of 900 mg. per 100 ml. or more. It is this factor which appears to be responsible for the very high E.S.R.

No remarkable changes are found in the bone-marrow; but occasionally the plasma cells are abundant (upper limits of normal) and some of them atypical, suggesting myelomatosis. Transient shadows may appear in the chest radiographs. There is no radiological change in the joints to suggest active arthritis, although some may show osteo-arthritic changes compatible with age. No matter how severe the illness may be, the ultimate prognosis is excellent, although aching and stiffness may persist for months or years with remissions.

DATA ON 21 CASES

Age (yr.):	
Male (4) mean 62·0, range 59–76	
Female (17) mean 67·0, range 56–82	
Pain in:	
Shoulder-girdle	21
Cervical spine	21
Lumbar spine	18
Other joints	13
Muscles	20
Chest	3
Abdomen	4
Transient swelling of joints	4
Loss of weight	17
Fever and sweating	12
Headache	8
Cough	5
Abdominal symptoms (flatulence, diarrhœa, &c.)	10
Skin nodules	3
Lymphadenopathy	5
Splenomegaly	1
Muscle and other biopsies: 1 of 7 had slight lymphocytic infiltration of dermis	
Miscellaneous features: 1 case had Sjogren's syndrome; 1 case had transient mitral systolic murmur	
E.S.R. (highest) (Westergren): mean 100 mm. in 1 hr., range 25–148 mm. in 1 hr.	
Hæmoglobin (lowest) (standard 14·8 g. per 100 ml.): mean 11·2 g. per 100 ml., range 7·7–14·5 g. per 100 ml.	
White-cell count: 3 had slight leucocytosis, 4 had abnormal white cells in peripheral blood	
Bone-marrow: 4 of 7 had slight plasmacytosis	
Blood-albumin level: mean 3·5 g. per 100 ml., range 4·2–2·9 g. per 100 ml.	
Blood-globulin level: mean 3·3 g. per 100 ml., range 2·3–5·2 g. per 100 ml.	
Plasma-fibrinogen level: mean 731 mg. per 100 ml., range 260–1240 mg. per 100 ml.	
Cryoglobulin: 3 of 11	
Electrophoresis of plasma-proteins: albumin decreased in 11 of 12, α-globulin fractions increased in 9 of 12	
Differential sheep-cell agglutination test: 3 D.A.T. 32 or over, 4 D.A.T. 16–32	
Urine: trace of protein in 4	
Chest radiography: transient shadows in 2	
Radiography of joints: none with active arthritis, mild osteo-arthritis in 10	
Salicylate response: 11 of 13	
Antibiotic response: none	
Duration: mean 5·25 yr., range 3 mos.–35 yr.	
Precipitating factor, physical or emotional stress: 8 of 21	

D.A.T., differential agglutination titre.

I propose to call the syndrome anarthritic rheumatoid disease. 2 typical cases are described below, and the group is summarised in the accompanying table.

Case-reports

Case 1.—A butcher's wife, aged 56, was admitted to the Radcliffe Infirmary in July, 1955, under Dr. F. G. Hobson, with four years' history of intermittent backache of such severity that she had to cling to the sides of her bed to turn over at night. She had occasional flitting pains in her interphalangeal joints and round her elbows. Two months before admission she had had retro-orbital and vertical headaches, felt tired, and sweated profusely at night. Her appetite was poor, and she had lost a stone in weight. Her doctor had repeatedly found a temperature of 100°F.

On examination she was pale and had angular stomatitis, temperature 99°F, pulse-rate 80, blood-pressure 130/80 mm. Hg, a few small lymph-nodes palpable in her neck and axillæ, some pain on flexing her spine, but no arthritis or other abnormality in any system.

Investigations.—E.S.R. 136 mm. in 1 hour (Westergren). White-cell count 7200 per c.mm. Repeated blood-cultures sterile. Agglutinations to salmonella and brucella negative. Chest radiograph and barium meal normal. Radiography of lumbar and sacral spine showed some osteo-arthritis but no ankylosing spondylitis. Occult blood was present on occasion in the stools but was not considered significant. The urine contained traces of protein now and then but no cells or casts. No lupus-erythematosus cells found. Blood-urea level 27 mg. per 100 ml. Plasma-proteins 7·0 g. per 100 ml. (albumin 3·4 g. per 100 ml., globulin 2·9 g. per 100 ml., fibrinogen 675 mg. per 100 ml.). Wassermann and Kahn reactions negative. Bone-marrow normal. Peripheral-blood films showed on occasion a circulating plasma cell. A muscle biopsy specimen was normal.

Progress.—The pyrexia, which did not respond to penicillin, streptomycin, or oxytetracycline, subsided after two months with some help from salicylates, and the patient was discharged.

Follow-up.—A month later she was much improved but still complained of a stiff and painful back. Her E.S.R. was 89 mm. in one hour (Westergren), hæmoglobin 12·8 g. per 100 ml., and white-cell count 5900 per c.mm. By January, 1956, she was almost symptomless, the E.S.R. had fallen to 42 mm. in one hour (Westergren), and the plasma-fibrinogen level to 400 mg. per 100 ml. A differential sheep-cell agglutination test was negative. The illness had lasted more than four years.

Case 2.—A school-teacher, aged 56, was admitted to the Radcliffe Infirmary in May, 1955, under Prof. L. J. Witts, with four months' history of pains in her arms, legs, neck, and shoulders. She had been profoundly upset by mice scampering over her at night in her infested bedroom and preventing her from sleeping. She had woken up one morning to find her knees, calves, shoulders, neck, and spine painful on movement. The pain was in her muscles and prevented her from sitting on a hard chair. She had night sweats and had lost nearly two stone in weight. She could not cope with her work and felt generally run down. There had been no swelling of her joints.

On examination her temperature was 99·8°F, pulse-rate 99, and blood-pressure 120/70 mm. Hg. She looked pale and had wasting of her limb muscles, which were tender on palpation. The joints and other systems were normal.

Investigations.—E.S.R. 122 mm. in one hour (Westergren). Hæmoglobin 11·2 g. per 100 ml. White-cell count 13,600 per c.mm. (slight neutrophil leucocytosis). Bone-marrow moderately cellular (plasma cells 2%). Plasma-proteins 7·8 g. per 100 ml. (albumin 3·3 g. per 100 ml., fibrinogen 1020 mg. per 100 ml.). Paper electrophoresis showed a slightly decreased albumin fraction and increased α_1 and α_2 globulin fractions. Wassermann and Kahn reactions negative. Paul-Bunnell test negative. No lupus-erythematosus cells seen. Agglutinations to salmonella and brucella negative. Blood-cultures sterile. Urine normal. Electromyogram, electrocardiogram, and radiographs of chest, hands, and wrists normal. Differential sheep-cell agglutination test negative. Biopsy of pectoral muscle showed slight œdema and scanty infiltration of the superficial dermis by lymphocytes, but the changes were too slight for scleroderma, and there was no evidence of any other collagen disease.

Progress.—In hospital the patient had persistent evening pyrexia (98·8–100·0°F) with tachycardia (80–100). She responded moderately well to salicylates. She was transfused for her anæmia and after a month lost most of her symptoms. By then her plasma-protein level was 7·2 g. per 100 ml. (albumin 2·9 g. per 100 ml., globulin 3·4 g. per 100 ml., fibrinogen 865 mg. per 100 ml.). Her illness had lasted about six months.

Laboratory Findings

Differential Sheep-cell Agglutination Test

Of 14 cases in the present series 5 gave a strongly positive reaction (differential agglutination titre 32 or more) and 4 a weakly positive reaction (differential agglutination titre 16–32). Although the test has been found positive in systemic lupus erythematosus, dermatomyositis, scleroderma, ankylosing spondylitis, osteo-arthritis, and "fibrositis" (Rose et al. 1948, Ball 1950, Svartz and Schlossmann 1952, Alexander and De Forest 1954) it is most frequently positive in rheumatoid arthritis. It was not found to be positive by the above-mentioned workers in rheumatic fever. This confirms the clinical findings that the syndrome resembles rheumatoid arthritis more than rheumatic fever.

Anæmia

Of the 21 patients reviewed here 15 had hypochromic iron-resistant anæmia at some time during their illness. This agrees with Jeffrey's (1953) findings in rheumatoid arthritis, where there seems to be some defect in the absorption of iron, with a low serum-iron level and an increased iron-binding capacity of the serum.

White-cell Count

In 3 cases there was a moderate leucocytosis, but in the 18 others the white-cell count was within normal limits. Abnormal white cells were found in the peripheral circulation in 3 cases, and in a 4th there was toxic granulation of the neutrophils.

Bone-marrow

Bone-marrow changes were not remarkable, but the finding of plentiful plasma cells up to the upper limits of the normal range, in 4 of 7 patients who underwent marrow puncture, nearly always suggested at first myelomatosis, as it did in case 1 of the previous series.

There may be an excess of plasma cells in the marrow in any condition with a raised plasma-globulin level, and this increase is in some way related to an antigenic stimulus provoking a plasma-cell response to produce globulin (Barr 1950). Houli and Monteiro Marinho (1954), investigating the bone-marrow of 20 cases of rheumatoid arthritis, found nothing remarkable apart from 7 cases with eosinophilia and 5 with plasmacytosis. 1 patient in my previous series also had eosinophilia. Jeffrey (1953) similarly found a mild plasmacytosis in 3 of 11 marrows from patients with rheumatoid arthritis.

Erythrocyte-sedimentation Rate

The lowest E.S.R. in the present series was 25 mm. in one hour and the highest 148 mm. in one hour (Westergren). In 10 of the 21 cases it was over 100 mm. in one hour, and in 14 it was 80 mm. or more in one hour. These are exceptionally high rates and form one of the characteristic features of the syndrome. Very often the constitutional changes are deceptively slight, and the high E.S.R. comes as a surprise when it is measured. In this respect the syndrome differs from rheumatic fever and other collagen diseases, where the highest E.S.R.s are found in profoundly ill patients. As a rule it is only in rheumatoid arthritis that the E.S.R. remains high in ambulant patients.

Plasma-proteins

Usually the albumin fraction was decreased and the globulin fraction increased. In 9 patients the globulin level was higher than the albumin level. The fibrinogen level was from 355 mg. to 1240 mg. per 100 ml.; it was above 1000 mg. per 100 ml. in 3 patients and above 800 mg. per 100 ml. in 5—a very high figure. The high fibrinogen level and E.S.R. are characteristic of the syndrome, and these findings in a patient outwardly suffering from "fibrositis" are usually sufficient to diagnose the condition.

Electrophoretic analysis of the plasma-proteins showed a decreased albumin fraction and a sharp increase in the α_1 and α_2 globulin fractions compared with the normal, and the γ-globulin fraction was occasionally slightly increased, but the over-all mean was within normal limits, and the β-globulin fraction only slightly above normal. A double β band was found on one occasion. Ropes et al. (1954) found the α-globulin fraction greater in rheumatoid arthritis than in systemic lupus erythematosus, in which the γ fraction was often very great.

3 patients had different amounts of cryoglobulins, the blood of 1 patient "gelling" at room-temperature. Holmberg and Grönwall (1942) described a cryoglobulin in rheumatoid arthritis, and it has been observed in numerous other conditions (Mackay et al. 1956).

Discussion

The classification of atypical rheumatic disorders is difficult, and the non-committal term "rheumatoid disease" is being increasingly used to denote them.

The characteristics which place the present cases in the rheumatoid group rather than in the group comprising systemic lupus erythematosus, polyarteritis nodosa, dermatomyositis, and scleroderma are the crippling muscular pains, the age-group, and the excellent prognosis.

Nodules may be found in both rheumatic disorders, but the partial rather than complete response to salicylates suggests that the syndrome is nearer to rheumatoid arthritis than to rheumatic fever.

Cranial arteritis occurs in a similar age-group to the patients described here and affects women more commonly than men. 8 of the present series had headache but this was not persistent, and the muscular pains eventually became the chief complaint. Although cranial arteritis is a generalised disease, the muscular aching is not so severe as in the present syndrome; moreover none of the seven biopsy specimens showed the characteristic pathology.

All the collagen diseases may be associated with a very high E.S.R.; all may have a reversal of the albumin/globulin ratio and hypochromic anæmia; in all the white-cell count may vary from a leucocytosis to a leucopenia; and in all there may be general malaise, loss of weight, and joint symptoms. It is, however, only in rheumatoid arthritis and in the closely related ankylosing spondylitis that pain in the muscles and joints is so severe as to make movement impossible.

In "fibrositis" (Slocumb 1936, Copeman 1949) the pain and stiffness are equally severe, but it is generally accepted that this is a condition without systemic upset and with normal E.S.R. Since many of the present patients had "fibrositis" when they were afebrile and a rheumatoid disorder when they were febrile, it is difficult to place a sharp dividing line, and we are left in doubt about where one condition begins and the other ends. Race (1940) emphasised this dilemma when he found a small group of his "fibrositis" patients with raised E.S.R. and thought that they behaved more like cases of rheumatoid arthritis. Slocumb (1936) also found some of his patients with a raised E.S.R. and anæmia, although they had no signs of a systemic disorder.

According to the Empire Rheumatism Council (1950) the prodromal symptoms of fatigue, loss of weight, transient joint pains, paræsthesiæ, migrant joint swellings, pyrexia, and sweating occurred in more than half the patients with rheumatoid arthritis, and they may be present for weeks or months before the joints are affected. In the present series 17 patients never progressed to arthritis, although they had all the other signs of rheumatoid arthritis.

Bauer (1939) described an atypical form of rheumatoid arthritis, coming on after some illness, with asymmetrical involvement of large joints and a migratory polyarthritis which may recover.

Several of the cases reported here were precipitated or made worse by illness, operation, or emotional stress.

Ropes and Bauer (1945) described another variant of rheumatoid arthritis with high pyrexia, various aches and pains in the back, hands, and legs, and paræsthesiæ. Articular, vasomotor, or non-articular symptoms may predominate, the last including skin, muscle, or bone atrophy, lymphadenitis, splenomegaly, iritis, pleurisy, pericarditis, rashes, and pigmentation.

Kersley (1954) collected 67 cases of atypical rheumatoid arthritis, some of which had an onset like rheumatic fever, but no carditis; others had only one joint affected. 5 cases showed gross destruction of bone on radiography but no pain.

Cecil and Kammerer (1951) were surprised how frequently the shoulders were affected in rheumatoid arthritis in the aged. Veikko et al. (1954) found that about half of 277 patients with rheumatic disorders had shoulder pain.

Schlesinger (1949), describing atypical rheumatoid arthritis in the young, emphasised the incidence of prolonged pyrexia and arthralgia, with or without arthritis.

There may be leucopenia or leucocytosis, hepatomegaly and splenomegaly, endocarditis, and encephalitis. It is difficult to distinguish this condition from systemic lupus erythematosus and polyarteritis nodosa.

Rheumatoid arthritis of the spine, a condition often overlooked and differing from ankylosing spondylitis (Bauer 1939), may produce similar symptoms to those found in the present series.

A syndrome in the elderly, similar to that described here but with more pronounced involvement of joints, was described by Kersley (1951); a high E.S.R., pyrexia, and a general constitutional disturbance were present. Unlike the present cases, however, the condition tended

to become chronic. Four biopsy specimens of muscle were normal.

Forestier and Certonciny (1953) reported 25 cases with bilateral symmetrical pains of sudden onset in the shoulders and hips, impaired movement, low pyrexia, and raised E.S.R. The prognosis was excellent. Because only the large joints were involved, these workers did not consider the condition to be rheumatoid arthritis and named it *pseudoarthrite rhizomélique*.

The rheumatoid disease of Ellman and Ball (1948), of widespread systemic nature, bears out the generalised nature of rheumatoid arthritis but does not strictly fall into the present group, because the joints were affected.

These variants of rheumatoid arthritis show that the disease may take many forms, some far removed from the classical pattern. In the anarthritic rheumatoid type described here the joints are not affected; once this has been recognised, this variant is found to be quite common.

Summary

A further 21 cases of a rheumatoid syndrome found in the middle-aged and elderly are described.

The characteristic feature was generalised aching of the muscles, especially of the neck, shoulders, and back.

In severe cases there were prolonged pyrexia, sweating, general malaise, wasting, headache, and abdominal symptoms.

The E.S.R. and plasma-fibrinogen level were exceptionally high, with a decrease in the blood-albumin and an increase in the α fractions of the blood-globulin. Cryoglobulins were present in 3 cases.

There was secondary iron-resistant anæmia. The white-cell count was usually within normal limits; abnormal white cells were found in the peripheral blood in 4 cases.

The bone-marrow sometimes showed plasmacytosis.

The symptoms and signs were similar to those of the prodromal stage of rheumatoid arthritis before the joints are affected. In 17 cases the joints were not affected.

4 cases with identical symptoms but with minimal transitory involvement of joints, form a link with true rheumatoid arthritis.

There was a fair response to salicylates.

The prognosis is invariably good, but the illness may persist for months or years with remissions.

It is suggested that this syndrome be called anarthritic rheumatoid disease.

I wish to thank Prof. L. J. Witts, Dr. F. G. Hobson, Dr. A. M. Cooke, and Dr. E. M. Buzzard for access to their patients and for reading the manuscript; Dr. A. M. Cooke for help and advice in connection with this paper; Mr. J. R. P. O'Brien; and the pathological and biochemical departments for those investigations which were not made by me.

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ADMINISTRATION OF LIVE INFLUENZA VIRUS TO VOLUNTEERS

A. ISAACS
M.D. Glasg.
MEMBER OF MEDICAL RESEARCH COUNCIL STAFF, NATIONAL INSTITUTE FOR MEDICAL RESEARCH, MILL HILL, LONDON

A. T. RODEN
M.D. Lond., D.P.H., D.C.H.
FORMERLY MEDICAL SUPERINTENDENT, COMMON COLD RESEARCH UNIT, SALISBURY

IMMUNISATION against epidemic influenza is normally carried out by subcutaneous inoculation of virus inactivated by formaldehyde. This procedure has on occasions given an approximately fourfold reduction in the incidence of clinical influenza in inoculated persons compared with uninoculated controls (Commission on Influenza 1944). But this degree of protection has not always been achieved, and in a trial in this country the incidence of clinical influenza in inoculated individuals was only 40% lower than that in controls given an antibacterial vaccine (Medical Research Council 1953). If a severe influenza pandemic were to break out, it is likely, in the present state of knowledge, that attempts would be made to produce large amounts of formaldehyde-inactivated vaccine from the prevailing strain of virus grown in chick embryos. With present techniques each dose of vaccine represents roughly the yield of virus from one egg, and the number of fertile eggs available would limit the amount of vaccine which could be produced rapidly. Burnet and Clark (1942) have pointed out that this difficulty could be circumvented if a live attenuated virus vaccine were developed, since, in theory at least, each egg might provide enough virus to immunise large numbers of people by the intranasal route.

In experiments with ferrets and mice it is easy to immunise against infection with virulent influenza virus by a preceding intranasal inoculation with live avirulent influenza virus. In man the results of experimental infection with influenza virus grown in the laboratory have been very variable, depending on the strain of virus, the technique of cultivation, the dosage used, and the pre-existing degree of immunity judged by the serum-antibody level before inoculation.

Smorodintseff et al. (1937) inoculated 72 volunteers intranasally with influenza virus grown in mouse lung. About 20% of the inoculated persons, particularly those with low initial antibody levels, had influenzal symptoms and an increase of neutralising antibody to the virus in their serum.

Chalkina (1938) gave repeated inhalations of ferret or mouse adapted virus to 272 men and noted that serum antibody appeared without clinical symptoms.

Burnet and Foley (1940) inoculated 15 volunteers consecutively with three strains of influenza virus A of increasing virulence at intervals of a week. 3 volunteers had a typical attack of influenza after the third inoculation, which was with a recently isolated virus, against which the previous inoculations of attenuated virus had not given any protection.

Francis (1940) injected 11 persons intranasally with tissue-cultures of the PR8 virus; there were no symptoms, and only 1 person had an increased amount of neutralising antibody.

Burnet (1942) sprayed large doses of influenza-B virus into the nose and throat of volunteers; symptoms were trivial, but many of the volunteers had an increased amount of antibody, especially those with a low initial antibody titre.

Similar experiments were made by Burnet (1943) and Mawson and Swan (1943) with a mixture of two influenza-A and one influenza-B strains, and by Bull and Burnet (1943) with influenza-B virus. Usually the symptoms following inoculation were slight; antibody responses occurred in about a third of those given the mixture of viruses and in a high proportion of persons with low initial antibody given the influenza-B virus.

Henle et al. (1943) inoculated each of 72 people of whom 44 had been previously vaccinated against influenza, with

RESULTS OF INOCULATION OF VOLUNTEERS WITH INFLUENZA-VIRUS STRAINS

Trial no. (date)	Volunteer no.	Age (yr.)	Virus inoculated		Inoculum	Clinical effect	Serum anti-hæmagglutinin		Serum-complement fixing titre		Tests for virus in garglings
			Strain	Passage			Pre-	Post-	Pre-	Post-	
1 (March 8, 1954)	1	35	A/Eng/1/53	Amn.1 All.10	$10^{5.5}$ egg-infective doses	Nil	<10	<10	8	8	1, 2, 3, 4, and 5 days after inoculation all negative
	2	32		,,	,,	,,	120	160	4	4	
	3	41		,,	,,	,,	<10	<10	4	4	
2 (Sept. 12, 1954)	4	21	A/Eng/1/53	Amn.1 All.10	$10^{5.6}$ egg-infective doses	Nil	20	20	8	8	2, 3, and 4 days after inoculation all negative
	5	23		,,	,,	,,	10	10	<5	<5	
3 (Nov. 23, 1954)	6	20	A/Eng/1/53	Amn.1 All.4	10^{5} egg-infective doses	Nil	40	40	3	3	2, 3, and 4 days after inoculation all negative
	7	20		,,	,,	,,	40	40	3	3	
	8	18		,,	,,	,,	15	15	4	3	
	9	21		,,	,,	,,	40	40	6	6	
4 (Jan. 3, 1956)	10	27	A/Eng/7/53	Amn.1 All.1	10^{4} egg-infective doses	Nil	15	<10	<10	<10	2 and 4 days after inoculation all negative
	11	23		,,	,,	,,	10	15	<10	<10	
	12	23		,,	,,	,,	<10	<10	<10	<10	
	13	19		,,	,,	,,	<10	<10	<10	<10	
	14	18		,,	,,	,,	20	20	<10	<10	
	15	22		,,	,,	,,	30	30	<10	<10	
	16	21		,,	,,	,,	20	30	<10	<10	
	17	21		,,	,,	,,	<10	<10	<10	<10	

about 0·45 ml. of undiluted allantoic fluid of an influenza-A virus culture. Of the 44 previously vaccinated persons, 1 developed symptoms of influenza, in contrast with 10 of the 28 in the unvaccinated controls.

Though these experiments have given much important information they do not tell us under what conditions the influenza virus, after cultivation in the laboratory, can multiply in man. The criteria which are usually taken to indicate that a virus has multiplied do not allow us to decide unequivocally that the influenza virus was multiplying in man in the experiments cited above. The development of an antibody response may be taken as evidence of multiplication of a virus only if the virus inoculum itself is insufficient to stimulate the production of antibody. In most of the investigations cited above the virus was administered in undiluted allantoic or amniotic fluid cultures in amounts which, if given as inactivated virus subcutaneously, might have been expected to produce an antibody response in a high proportion of people (Hirst et al. 1942, Salk 1947). The occurrence of clinical symptoms resembling influenza seems to afford presumptive evidence of multiplication of the virus, particularly in the experiments of Burnet and Foley (1940) in which the recently adapted virus produced symptoms whereas the attenuated virus did not. However, Salk (1948) has shown that large doses of formalin-inactivated influenza virus given subcutaneously can produce symptoms resembling a moderately severe attack of influenza. Live virus may possibly be more potent in this respect; and, since the toxic effect of large doses of virus, after intravenous or intranasal infection of mice, is well known (Henle and Henle 1946, Sugg 1949), one cannot be certain that the development of symptoms in man after intranasal inoculation of large doses of virus is evidence that the virus has multiplied. In the studies of Burnet and Foley (1940) and Bull and Burnet (1943) virus was recovered from the volunteers two days after inoculation. Although this might be accepted as evidence of multiplication of the virus it could also be interpreted as survival of virus from the original inoculum, since quantitative estimations were not recorded. Smorodintseff et al. (1937) recovered virus from volunteers immediately after inoculation, but the amount of virus recovered subsequently decreased steadily, and no virus was detected three days after inoculation. They interpreted this as indicating that, after adaptation to ferrets and mice, the virus was unable to multiply in man.

The aim of the present investigation was to prepare influenza virus which would multiply in man without producing symptoms. The viruses used were recently isolated strains of influenza-A virus after not more than 10 passages in the allantoic cavity of the chick embryo; the passage level tested was reduced as the clinical trials proceeded. Volunteers were inoculated with a dilution of virus which was estimated to be insufficient in itself to produce either symptoms or an antibody response. Particular attention was paid to the development of antibody to the "soluble antigen" (Hoyle and Fairbrother 1937), which would indicate multiplication of the virus.

Materials and Methods

Viruses.—A/England/1/53 and A/England/7/53 strains of influenza virus were isolated in 1953 after a single amniotic passage in chick embryos and maintained thereafter by allantoic passages. The virus was stored as allantoic fluid in sealed capillary tubes at −70°C and diluted in 50% broth (Hedley-Wright) in saline solution before administration to volunteers.

Serological Tests.—Sera from volunteers were tested for their content of antihæmagglutinin to the virus administered and for antibody to influenza-virus-A soluble antigen by techniques previously described from this laboratory (see World Health Organisation 1953).

Recovery of Virus.—Garglings were obtained in saline solution to which bacteriological broth, to a concentration of 20%, was added. The garglings were stored at −70°C and were thawed out immediately before testing for the presence of virus. After the addition of penicillin and streptomycin 0·1-ml. volumes were inoculated into the amniotic cavity of 13-day chick embryos. Fluids were harvested after 5 days' incubation at 35°C and tested for agglutinins for chick and guineapig erythrocytes. In addition, 10-day embryos received inoculations into the allantoic cavity, and the allantoic fluids were tested for agglutinins for fowl erythrocytes after 3 days' incubation.

Experimental

Volunteers were accommodated at the Common Cold Research Unit, Harvard Hospital, Salisbury, in groups of two, three, or four, with isolation precautions as described by Andrewes (1949).

A medical examination, including radiography of the chest, was made of each volunteer to ensure general physical fitness for participation in the trial. The volunteers wrote a daily report of symptoms, if any, and the clinical observer examined them daily for signs of respiratory infection. Body-temperatures and pulse-rates were recorded twice daily.

After a preliminary period of observation of 2–3 days the preparation of virus was administered, in quantities of 0·5–1·0 ml. of an appropriate dilution, by intranasal instillation in the first trial and by pharyngeal spray in subsequent trials. Daily clinical observations were maintained for 7 days after the administration. Before leaving the Unit each volunteer was given a postcard questionnaire to be completed and returned 2 weeks after departure.

Garglings were collected in each case on the 2nd and 4th days after administration of virus and, in some cases, on the 1st, 3rd, and 5th days also. Specimens of blood were taken before the administration and again 2–3 weeks after. The sera were stored at –70°C and inactivated by heating at 56°C for 30 minutes before testing.

Results

17 volunteers participated in four separate trials; 2 additional volunteers were excluded from trial 2 because of symptoms of upper respiratory infection in the preliminary observation period. The results are shown in the accompanying table.

The table shows that, after administration to volunteers of between 10^4 and $10^{5\cdot6}$ egg-infective doses of influenza-A virus, either intranasally or by throat spray, no symptoms suggesting acute respiratory infection developed either during the period of observation or during the fortnight after departure. No significant increase in serum-antihæmagglutinin or complement-fixing antibody was observed, and no virus was recovered in garglings collected after inoculation. The virus used in trial 4 had been grown for one amniotic and one allantoic passage and gave an infectivity titre ten times higher when titrated by the amniotic than by the allantoic route. Although this virus may be considered as incompletely adapted to growth in the allantoic cavity of the chick embryo it showed no evidence of multiplication in man. On the basis of these trials with a small number of volunteers it appears that influenza virus, on passage in the allantoic cavity of the chick embryo, may rapidly lose its power to multiply in man.

Discussion

The possibility of using live influenza virus for immunisation may be considered in two stages. First, can influenza virus be prepared in a form in which it will multiply in man without producing symptoms?

Reasons have been given above for considering that the question whether influenza virus, after cultivation in the laboratory, can multiply in man cannot be answered from a knowledge of published work on the subject. The results of the present investigation suggest that, on passage in the allantoic cavity of the chick embryo, influenza virus may rapidly lose its power to multiply in man.

In similar recent experiments made by Dr. W. H. Price of Baltimore, U.S.A. (personal communication), 40 volunteers were inoculated intranasally with 30,000–3,000,000 tissue-culture doses of recently isolated influenza-A virus in the first amniotic passage. Of these volunteers 60% developed influenza, and four-fifths of the remainder showed antibody responses similar in magnitude to those observed in the volunteers with clinical evidence of infection. It was concluded from the amounts of virus recovered from volunteers that the virus had multiplied.

Details of these experiments are awaited with great interest, and it would be most interesting to compare the behaviour of virus grown in the amniotic cavity of the chick embryo with that of the same virus after a single passage in the allantoic cavity. The results described by Dr. Price, in conjunction with the results of the present investigation, conform to the suggestion made by Burnet and Bull (1943) that influenza-A virus isolated in the amniotic cavity in the "O," or original, phase resembles the virus as it occurs in man, whereas on passage in the allantoic cavity it changes to the "D," or derived, phase in which it may become attenuated for man. Further experiments are needed to test this hypothesis.

The studies of Mogabgab et al. (1956) suggest that some indication of the ability of influenza viruses to multiply in man might be obtained by studies of their multiplication in cultures of human tissue. This is one of several methods which might be applied to the problem of whether virus can be prepared from any influenza strain in a form in which it will multiply in man without producing symptoms. If this can be achieved, the second stage—consideration of the question whether such a virus would protect against natural influenza infections—can then be studied.

Summary

17 volunteers were inoculated intranasally or by throat spray with live influenza-A virus prepared by one amniotic passage and either one, four, or ten allantoic passages in chick embryos. The inoculum contained between 10^4 and $10^{5\cdot6}$ egg-infective doses.

No symptoms of respiratory infection developed, no virus was recovered from the volunteers, and no increase in either serum antihæmagglutinin or in antibody to the influenza "soluble" antigen was observed.

It was concluded that, on passage in the allantoic cavity of the chick embryo, the virus rapidly lost its ability to multiply in man.

We wish to thank the volunteers; Dr. C. H. Andrewes, F.R.S., for advice and criticism; the Medical Research Council's Committee on Clinical Trials of Influenza Vaccine, particularly the secretary, Brigadier A. E. Richmond, who helped to recruit volunteers; and Dr. W. H. Price for allowing us to cite results of his unpublished experiments.

ADDENDUM

Dr. C. H. Andrewes has informed us, on his return from attendance at the 13th All-Union Congress of Hygienists, Epidemiologists, Microbiologists and Infectionists in Leningrad, of work in this field in the U.S.S.R.

Prof. A. A. Smorodintseff and Prof. V. D. Soloviev have for some years been working with a living attenuated influenza vaccine. Suitable strains are selected for their ability to persist in noses of adult human beings and to immunise as a result. They are administered, in dilutions of 1 in 5 or 1 in 10 allantoic fluids, either as coarse spray or powder. They cannot be given thus to young children, because 20% have influenza-like reactions. Twofold to fivefold reduction in incidence of influenza is claimed, but vaccination must be repeated yearly.

It is assumed that this virus can multiply in man, because it has been recovered in a dilution of 10^{-4} from inoculated persons—a finding which is unlikely to be due to survival of virus from the original inoculum. However, it is not clear why it should be necessary to administer the vaccine in such high concentration if the virus can multiply in man; nor is it clear what advantage the live vaccine in its present form has over a killed-virus vaccine.

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ABSORPTION IN SPRUE OF VITAMINS OF THE B COMPLEX

RONALD H. GIRDWOOD
M.D., Ph.D. Edin., F.R.C.P.E., F.R.C.P.
SENIOR LECTURER IN MEDICINE, UNIVERSITY OF EDINBURGH

IN previous papers (Girdwood 1953, 1956) it was shown by means of a differential test of urinary folic-acid excretion that malabsorption of folic acid is a very common feature in idiopathic steatorrhœa and related conditions. In this test the urinary output of folic acid is estimated after subcutaneous and oral doses of 5 mg. of synthetic pteroylglutamic acid; in idiopathic steatorrhœa and related conditions in relapse, but not in other diseases, the urinary output of folic acid after the oral dose is significantly less than after the injected dose.

In the present preliminary investigation the absorption of certain other members of the vitamin-B complex was studied by microbiological methods similar to those employed in the differential urinary folic-acid-excretion test. Unfortunately this test is not suitable for measuring the absorption of vitamin B_{12}, which is at present being investigated by means of radioactive isotopes. The excretory products in the urine after test doses of nicotinic acid or nicotinamide are very largely N'-methylnicotinamide and other methylated forms. Since these cannot be assayed microbiologically their measurement was not attempted in this preliminary investigation.

Methods

The vitamins studied in the investigation were folic acid, riboflavine, aneurine, and pyridoxine.

In each instance the patient was given subcutaneously a measured amount of the vitamin under investigation from a specially prepared batch, the potency of which I had checked microbiologically. The urine was collected for 24 hours, and thereafter the same dose of the same batch was given by mouth and the urine again collected for 24 hours. All specimens were collected and preserved under toluene in brown bottles, and for the riboflavine and aneurine collections the bottles also contained glacial acetic acid.

The specimens were kept in a refrigerator at 4°C. The tests were usually carried out within a week. Recovery experiments with vitamins added to the urine gave satisfactory results.

The doses of vitamins administered in each instance were: pteroylglutamic acid 5 mg., riboflavine 10 mg., aneurine 25 mg., and pyridoxine 50 mg.

The quantities of the vitamins excreted in the urine were estimated microbiologically by the methods indicated below, turbidity measurements of the extent of growth of the test organisms being made with a Spekker photo-electric absorptiometer.

Pteroylglutamic acid.—Test organism *Streptococcus fæcalis*. The medium was that of Teply and Elvehjem (1945). Incubation was for 16 hours at 37°C.

Riboflavine.—Test organism *Lactobacillus helveticus*. The medium was that of Barton-Wright (1945). Incubation was for 16 hours at 37°C.

Aneurine.—Test organism *L. fermenti*. The medium was that of Fitzgerald and Hughes (1949). Incubation was for 18 hours at 37°C. This microbiological method does not measure pyramin, which is a pyrimidine-like product of aneurine excreted in the urine. When the dose of aneurine given is as large as 25 mg., the substance excreted in the urine is largely aneurine (Alexander et al. 1946) and hence the failure to estimate pyramin excretion does not invalidate this method of investigation.

Pyridoxine.—Test organism *Neurospora sitophila*. The medium was that of Barton-Wright (1952). Incubation was for 5 days at 30°C. The forms of vitamin B_6 that this method measures include pyridoxine, pyridoxal, and pyridoxamine, but not 4-pyridoxic acid, the predominant metabolite to appear in the urine whether vitamin B_6 is given as pyridoxine, pyridoxal, or pyridoxamine. Measurement of 4-pyridoxic acid is done fluorometrically. It was thought that measurement of these three forms alone would be sufficient to show any difference in the absorption and excretion of vitamin B_6 in sprue patients.

Cases 2, 6, 7, 9, and 10 had had folic-acid treatment and cases 2 and 9 had had multivitamin tablets before the tests were carried out.

Results

The results of the investigation are given in the accompanying table.

URINARY OUTPUT OF VITAMINS AFTER TEST DOSES BY INJECTION AND BY MOUTH

Case no.	Sex	Age (yr.)	Diagnosis	Duration of illness	Hb level (g. per 100 ml.)	Serum-vitamin-B_{12} (µµg. per ml.) *L. leichmannii*	Urinary output: Folic acid (mg.) after 5 mg. dose		Riboflavine (mg.) after 10 mg. dose		Aneurine (mg.) after 25 mg. dose		Vitamin B_6 (mg.) after 50 mg. pyridoxine	
							A	B	A	B	A	B	A	B
1	F	64	Idiopathic steatorrhœa	4 mos.	2·1	..	1·53	0·20	5·4	6·4	7·5	1·5	3·7	2·4
2	M	45	Tropical sprue	11 yr.	17·0	320	3·20	0·21	7·0	4·4	4·0	1·1	3·4	4·1
3	M	46	" "	8 mos.	11·4	320	1·20	0·32	6·6	7·2	3·4	1·4	3·9	3·2
4	M	72	" "	2 yr.	3·3	180	0·91	0·36	7·1	2·6	7·6	2·8	2·0	1·6
5	M	35	Tabes mesenterica	2 mos.	8·0	250	1·35	0·42	2·1	3·6	12·1	1·4	4·4	4·5
6	M	43	Idiopathic steatorrhœa	10 yr.	11·7	150	1·52	0·43	3·7	5·4	13·0	4·0	3·4	3·1
7	F	54	" "	4 yr.	12·8	300	1·97	0·53	4·4	3·7	6·7	1·7	3·8	2·4
8	M	47	Diabetes and steatorrhœa	7 yr.	9·4	..	2·22	0·67	6·0	6·3	5·0	1·2	2·7	3·2
9	F	45	Idiopathic steatorrhœa	5 yr.	7·5	270	3·91	0·85	7·2	4·9	2·9	0·9	3·4	4·9
10	M	22	" "	6 yr.	11·0	280	4·13	1·22	3·5	2·2	11·5	4·7	4·3	3·2
11	M	39	Blind loop (small intestinal)	15 yr.	10·4	..	3·36	1·70	4·6	6·7	5·3	2·7	2·3	2·6
12	M	21	Ileo-transverse colostomy	3 yr.	12·6	150	0·78	2·44	7·5	7·8	6·9	4·6	2·1	2·3
13	M	55	Gastro-enterostomy	6 yr.	11·6	<50	2·19	1·89	7·4	8·9	3·4	1·0	..	..
14	F	68	Pernicious anæmia	9 mos.	7·3	<50	0·60	1·91	2·4	6·4	7·2	1·5	2·8	4·6
15	F	71	" "	4 yr.	6·4	<50	1·91	2·10	4·4	7·5	8·7	1·2	3·0	4·2
16	F	59	" "	1½ yr.	13·0	<50	2·89	2·18	3·3	5·4	13·6	1·5	4·4	5·4
17	F	55	" "	6 mos.	6·0	<50	1·51	2·49	6·4	2·6	12·1	2·1	5·1	4·5
18	F	60	Diabetic neuritis	5 mos.	10·9	300	..	..	5·9	1·7	5·9	2·1	2·7	1·5
19	F	53	Bleeding duodenal ulcer	3 weeks	11·2	..	3·89	1·80	5·4	2·6	2·9	1·1	2·4	2·5
20	F	44	Hyperparathyroidism	2 yr.	9·6	..	4·04	2·12	2·5	2·5	14·4	1·4	4·3	4·3
21	F	53	Scleroderma	20 yr.	10·0	..	3·96	2·41	5·6	5·0	7·3	2·4	1·7	2·9
22	F	37	Bleeding diathesis	30 yr.	10·0	..	3·22	3·09	2·0	3·1	9·0	2·9	2·1	2·5
23	F	24	Hæmoptysis	2 weeks	14·8	..	2·58	3·38	3·1	3·2	18·6	1·6	3·0	5·5
24	F	76	Coronary thrombosis	4 weeks	15·0	..	4·01	3·42	6·6	6·7	13·1	2·6	7·3	7·3
25	F	30	Duodenal ulcer	4 yr.	13·0	..	3·09	3·75	4·8	5·4	14·7	1·9	6·2	5·0
26	F	68	Senile osteoporosis	6 yr.	14·2	..	4·20	3·85	3·5	5·3	8·7	3·1	2·7	5·6

A, Output after subcutaneous dose. B, Output after oral dose.

Folic Acid

It will be seen that, as in cases already reported (Girdwood 1956), the urinary output of folic acid in patients with idiopathic steatorrhœa and tropical sprue was considerably less after the oral dose of 5 mg. of folic acid than it was after the injected dose; in cases 1–10 (" sprue ") the output after the oral dose was less than 1·5 mg. in all instances, whereas in cases 11–26 (controls) it exceeded this figure. The mean figures for urinary excretion of folic acid are :

Cases 1–10 (" sprue ") :	Output after	injected dose	2·19 mg.
	,, ,,	oral ,,	0·52 mg.
*Cases 11–26 (controls) :	Output after	injected dose	2·75 mg.
	,, ,,	oral ,,	2·57 mg.

* Excluding case 18, where the collection was incomplete.

Malabsorption of folic acid is therefore a feature of cases 1–10.

When the other vitamins are considered, however, it will be seen that no evidence of malabsorption was found. The mean figures are as follows :

Riboflavine

Cases 1–10 (" sprue ") :	Output after	injected dose	5·3 mg.
	,, ,,	oral ,,	4·7 mg.
Cases 11–26 (controls) :	Output after	injected dose	4·7 mg.
	,, ,,	oral ,,	5·1 mg.

Aneurine

The mean figures are :

Cases 1–10 (" sprue ") :	Output after	injected dose	7·4 mg.
	,, ,,	oral ,,	2·1 mg.
Cases 11–26 (controls) :	Output after	injected dose	9·5 mg.
	,, ,,	oral ,,	2·2 mg.

Thus the urinary output after the oral dose was less than after the injected dose in the " sprue " cases, but this is also the case with the controls.

Pyridoxine (including pyridoxal and pyridoxamine)

The mean figures are :

Cases 1–10 (" sprue ") :	Output after	injected dose	3·5 mg.
	,, ,,	oral ,,	3·3 mg.
*Cases 11–26 (controls) :	Output after	injected dose	3·5 mg.
	,, ,,	oral ,,	4·1 mg.

* Excluding case 13 owing to technical difficulties with the assay.

In all the " sprue " cases where it was estimated, the serum-vitamin-B_{12} level exceeded 130 μμg. per ml., the lower limit of normal by the assay method employed. This does not, however, necessarily indicate that absorption of vitamin B_{12} was normal in all these patients, since in certain conditions (e.g., total gastrectomy) malabsorption of vitamin B_{12} may be demonstrated by radioactive techniques months or even years before the consequent development of a lowered serum-vitamin-B_{12} level or of megaloblastic anæmia attributable to deficiency of vitamin B_{12}.

Conclusion

With the dosages and methods used in this investigation it has not been possible to show in ten cases of idiopathic steatorrhœa and related diseases that malabsorption of folic acid is accompanied by impaired absorption of riboflavine, aneurine, or pyridoxine.

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CLINICAL FEATURES OF ASEPTIC MENINGITIS CAUSED BY COXSACKIE-B VIRUS *

D. L. McLEOD
M.D. Toronto
POLIOMYELITIS RESEARCH FELLOW

A. J. BEALE
M.D. Lond., Dip. Bact.
RESEARCH FELLOW IN VIRUS DISEASES

G. A. McNAUGHTON
M.D. Toronto
CHIEF, INFECTIOUS SERVICE

A. J. RHODES
M.D. Edin., F.R.C.P.E.
DIRECTOR, RESEARCH INSTITUTE

HOSPITAL FOR SICK CHILDREN, TORONTO

ASEPTIC meningitis in summer is usually ascribed to non-paralytic poliomyelitis. Although it is well known that other viruses may cause the syndrome, it has been generally believed that poliomyelitis virus is the commonest cause in North America. Improved technical methods for the study of viruses have shown, however, that many such cases are caused by Coxsackie-B viruses; the evidence incriminating these agents has been reviewed by Rhodes and Beale (1956).

Since 1950, in the Hospital for Sick Children, Toronto, we have studied seventeen cases of aseptic meningitis caused by Coxsackie-B virus. All these cases were adequately studied to exclude concurrent infection with poliomyelitis. We describe here the clinical features of these cases of proved Coxsackie-B meningitis. One of our objectives was simplification of the differential diagnosis for the attending physician, but we did not attain it.

Cases Studied

All the cases were admitted to the Infectious Service of the Hospital for Sick Children with a diagnosis of non-paralytic poliomyelitis or of aseptic meningitis. A detailed clinical history was taken and an examination was made on admission by a research fellow. Most cases were followed after discharge, when convalescent sera were collected. On, or as soon as possible after, admission stools, blood, and cerebrospinal fluid (C.S.F.) were collected for virus studies. The techniques of examination for viruses included the inoculation of suckling mice, monkeys, and monkey-kidney monolayer tissue-cultures by standard methods previously described in detail by Beale et al. (1956).

Results

Virus Studies

The evidence incriminating Coxsackie-B virus as the cause of the illness in these seventeen patients is presented in table I. Every patient except case 1 yielded a Coxsackie-B virus that could be assigned to one of Dalldorf's antigenic types. It will be seen that in 1950 one B1 strain was isolated. Six patients yielded B2 virus during 1951, 1954, and 1955. Nine patients, all seen in 1952, yielded B4 virus. Three patients (cases 8, 10, and 15) excreted the same antigenic type of virus in stools and C.S.F.; two of these strains were B4 and one B2.

Ten of the twelve patients who provided suitable samples of serum showed during convalescence a rise in antibody to the homologous Coxsackie virus isolated from stools. Neutralising antibody titres to the three

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TABLE I—SEVENTEEN CASES OF ASEPTIC MENINGITIS CAUSED BY COXSACKIE-B VIRUS: LABORATORY DIAGNOSIS

Month and year of illness	Case no.	Age (yr.)	Sex	Coxsackie-B virus isolated from stool			Coxsackie-B virus in C.S.F.		Neutralising Coxsackie antibody *		Poliomyelitis virus in stool		
				Mice	"Maitland" cultures	Monkey-kidney monolayers	Mice	Monolayers	Acute serum	Convalescent serum	Monkeys	"Maitland" cultures	Monkey-kidney monolayers
July, 1950	1	9	M	+	..	..	..	..	No serum	No serum	–	..	..
Aug., 1950	2	6	M	+ (B1)	..	..	..	..	0·8	2·6	–	..	..
July, 1951	3	11	M	+ (B2)	..	..	..	..	1·5	1·2	–	..	..
July, 1952	4	7	F	+	–	+(B4)	–	–	2·4	4·1	–	–	–
July, 1952	5	4	F	+	+	+(B4)	–	–	1·9	3·1	–	–	–
July, 1952	6	5	F	+	+	+(B4)	–	–	0·3	1·9	–	–	–
July, 1952	7	4	F	+	+	+(B4)	–	–	No serum	No serum	–	–	–
Aug., 1952	8	6	M	+	–	+(B4)	–	+(B4)	0·2	2·2	–	–	–
Aug., 1952	9	7	M	+	+	+(B4)	–	–	2·1	2·1	–	–	–
Aug., 1952	10	4	F	+	+	+(B4)	–	+(B4)	1·8	2·5	–	–	–
Aug., 1952	11	7	M	+	+	+(B4)	–	–	No serum	No serum	–	–	–
Aug., 1952	12	10	F	+	–	+(B4)	–	–	2·0	3·0	–	–	–
Aug., 1954	13	6	F	+	..	+(B2)	..	–	–	–	..	..	–
Aug., 1954	14	4	M	..	..	+(B2)	..	–	No serum	No serum	..	..	–
Sept., 1954	15	5	F	..	..	+(B2)	..	+(B2)	1·3	2·9	..	..	–
Oct., 1954	16	7	F	+	..	+(B2)	..	–	1·1	1·6	..	..	–
June, 1955	17	6	M	..	..	+(B2)	..	–	< 0·5	2·5	..	..	–

* Expressed as negative logarithm of the 50% neutralisation titre in terms of final serum dilution.

types of poliomyelitis virus were done on nine patients (table II). It will be seen that three patients (cases 5, 9, and 10) had antibody for only one type of virus; none of these patients showed a significant rise in antibody titre.

Fourteen of the cases were seen in July or August, and one each in June, September, and October.

Clinical Features

There were eight males and nine females. The average age was 6 years; no cases were seen in children aged less than 4 years or more than 11 years. The chief clinical features are shown in table III. The patients usually attended hospital shortly after an abrupt onset of symptoms referable to meningeal irritation. Eleven patients had a history of prodromal illness. The prodromal phase merged into the major phase of the disease without a period of freedom from symptoms in nine patients. In two patients (cases 8 and 10) there was a short asymptomatic apyrexial period between the two phases of the "dromedary" illness. Malaise, anorexia, and "crampy" epigastric pains were prominent features of the prodromal illness. Six patients had no prodromal illness.

The frequency of the main features of the major phase of the illness is shown in table IV. Pyrexia was a constant finding. Nausea or vomiting, headache, and drowsiness were often present. Clinical signs of meningitis were elicited in 15 patients. Muscle tenderness or myalgia was present in seven cases, but in no case did this present as pleurodynia. Case 5 had a convulsion.

TABLE II—ASEPTIC MENINGITIS CAUSED BY COXSACKIE-B VIRUS: SERUM ANTIBODY TITRES FOR THE THREE TYPES OF POLIOMYELITIS VIRUS.

Case no.	Days after onset serum collected		Poliomyelitis antibody titres*					
			Type 1		Type 2		Type 3	
	S_1	S_2	S_1	S_2	S_1	S_2	S_1	S_2
4	1	33	1·3	1·3	2·0	2·1	1·8	1·8
5	3	36	0·3	0·3	0·3	0·3	2·8	3·2
6	3	39	1·3	1·3	2·8	2·4	1·8	1·8
8	0	35	1·3	1·3	1·3	1·3	1·3	1·3
9	1	34	0·3	1·3	0·9	0·8	1·8	1·8
10	4	36	0·3	1·3	0·3	1·3	1·6	1·6
12	2	38	0·3	0·3	2·5	2·7	2·5	2·7
15†	..	10	..	1·0	..	1·0	..	1·0
17†‡	4	72	1·5	0·6	1·5	0·9	1·2	0·6

* Expressed as negative logarithm of final dilution of serum protecting 50% of cultures.
† Poliomyelitis antibody titres determined by pH inhibition method and expressed as negative logarithm of initial dilution of serum giving complete protection.
‡ Received two doses of formalinised poliomyelitis vaccine four weeks before current illness.

No case developed paralysis during the acute phase; no residual weakness was detected in convalescence. The deep and superficial reflexes were normal in all the patients, and no patient had muscular tremor.

The clinical laboratory findings are shown in table III. The white-cell count was moderately raised, the average being 9300 per c.mm. Cells were present in the C.S.F. in all the cases, nine had between 11 and 100 cells per c.mm., six between 101 and 500, and only two over 500 cells. The average count was 171 cells per c.mm. Lymphocytes and polymorphs were present in about equal numbers in seven cases, lymphocytes predominated in eight cases, and polymorphs in three cases. The protein values were normal or slightly raised, and the chloride and sugar levels were normal.

Discussion

The syndrome of aseptic meningitis is caused by a wide variety of ætiological agents (Rhodes 1955). In North America the main viral agents that have been implicated are poliomyelitis, Coxsackie-B, mumps, herpes-simplex, lymphocytic-choriomeningitis, and more recently "orphan" or "Echo" viruses. Certain bacterial infections may simulate virus meningitis, particularly leptospirosis, tuberculosis, and antibiotic-treated cases of purulent meningitis (Fanconi 1951).

Mumps may present as aseptic meningitis and run its course without parotitis. There is usually a history of contact with cases of parotitis. The clinical laboratory findings are often distinctive (Adair et al. 1953). Thus the cell-count, though variable, is usually higher than in Coxsackie-B meningitis, being about 400 cells per c.mm.; the cells are mainly mononuclears. The protein content is usually slightly increased. The determination of the serum-amylase level may be helpful, for it is believed to be raised in mumps meningitis, even in the absence of parotid swelling (Wallman and Vidor 1955).

Lymphocytic-choriomeningitis is rare in Canada. There is often a localised outbreak among persons in close contact with infected mice. The C.S.F. findings are often characteristic (Adair et al. 1953), for the mean cell-count is about 700 per c.mm. The C.S.F.-protein level is raised, and the sugar content is usually significantly lowered.

Herpes-simplex meningitis is also rare in Canada. It is usually severe, with signs of encephalitis. The diagnosis depends on isolating the virus or demonstrating a rise in titre of antibodies during convalescence.

The differentiation between poliomyelitis, Coxsackie-B, and Echo virus infection is more difficult. Any muscular weakness, alteration of the reflexes, or tremor suggests poliomyelitis because these signs are noted in the pre-

TABLE III—SEVENTEEN CASES OF ASEPTIC MENINGITIS DUE TO COXSACKIE-B VIRUS: SYMPTOMS AND CLINICAL LABORATORY FINDINGS

Case no.	Duration of illness (days)		Onset of major phase till admission (days)	Main features						Laboratory findings on admission				
											C.S.F.			
	Prodromal phase	Major phase		Headache	Drowsiness	Nausea and vomiting	Myalgia	Signs of meningitis	Temperature on admission (°F)	White blood-cells (per c.mm.)	Cells (per c.mm.)	Lymphocytes per 100 total cells	Protein (mg. per 100 ml.)	Sugar (mg. per 100 ml.)
1	3	3	1	+	+	+	+	−	100	6000	120	100	..	..
2	3	2	1	+	−	−	+	+	103·4	7500	15	10	24·2	..
3	6	2	2	−	+	−	−	+	102	6200	18	90	..	..
4	..	3	0	+	+	+	−	+	104	14,100	29	60	..	..
5	..	3	0	−	+	+	−	+	101·4	9000	40	100	22·4	72·2
6	..	4	0	+	+	+	−	+	101·4	15,600	204	90	44·6	57·4
7	..	3	0	+	−	+	+	+	102	8000	50	40	16·1	76·0
8*	4†	2	1	−	+	+	−	+	100·2	6500	700	33	38·9	61·2
9	5	3	1	+	−	+	+	+	100·4	7000	100	80	14·7	66·8
10*	2†	3	1	+	+	+	−	+	102·4	16,200	325	30	20	54
11	5	3	1	+	−	+	−	+	103	6200	181	60	..	70
12	4	3	2	+	+	+	+	−	100	6200	106	34	23·3	..
13	..	4	0	+	+	+	−	+	104	7600	86	84	..	..
14	2	3	1	−	+	+	−	+	103	9800	240	25	22·1	74
15*	..	4	1	+	−	+	−	+	100·2	9600	36	90	..	..
16	3†	4	0	+	+	+	−	+	102	15,000	600	15	17	76·5
17	3	4	3	−	+	−	+	+	101	7600	90	100	..	..

* These patients excreted Coxsackie-B virus in the C.S.F.
† In these patients there was a short symptom-free period between the two phases of illness.

paralytic phase of cases proceeding to paralysis. Virus studies have shown that poliomyelitis virus is not a very common cause of aseptic meningitis in Toronto. At the Hospital for Sick Children 18 of 96 cases of aseptic meningitis or "non-paralytic" poliomyelitis seen in 1950–55 yielded poliomyelitis virus, although the virus was recovered from 85% of paralytic cases during the same period (Rhodes 1956). The seventeen cases of Coxsackie-B meningitis now described were seen during the same period and would have been diagnosed as "non-paralytic" poliomyelitis but for virus studies.

In Sweden (Gard 1954, Johnsson 1955) and South Africa (Bayer and Gear 1955) cases of Coxsackie-B meningitis have been described with concomitant pleurodynia. We have not, however, noted this in our patients. Johnsson (1955) also stated that intermittent fever was a prominent feature. Only two of our eighteen cases showed this type of febrile course.

TABLE IV—SEVENTEEN CASES OF ASEPTIC MENINGITIS CAUSED BY COXSACKIE-B VIRUS: FREQUENCY OF CLINICAL FEATURES OF THE MAJOR PHASE

Feature	No. of cases
Fever	17
Clinical signs of meningitis	15
Nausea and vomiting	14
Headache	13
Drowsiness	12
Pain in neck and back	11
Myalgia	6
Convulsions	1

It is clear that some "orphan" or Echo (National Foundation for Infantile Paralysis Committee 1955) virus strains may cause aseptic meningitis, since we have isolated viruses of this type from the C.S.F. of two patients (Duncan et al. 1955). As yet too few cases have been described to justify a description of the clinical features. There are indications, however, that transient weakness of muscle may occur, particularly in infection with Echo-virus type 6 infection (Karzon et al. 1956).

Conclusions

It is usually impossible to make a clinical diagnosis of Coxsackie-B meningitis in an individual case, the pathognomonic sign of pleurodynia being rare. The very absence of localising signs may offer suggestive evidence by exclusion. A knowledge of the prevalent disease in the community may suggest the likely diagnosis, a case of aseptic meningitis being likely to be due to Coxsackie-B, poliomyelitis, or mumps virus if pleurodynia, paralytic poliomyelitis, or mumps is present in the community. Even during epidemics of paralytic poliomyelitis, however, there is evidence that some cases of aseptic meningitis are not due to poliomyelitis (Svedmyr et al. 1956).

The great technical advances taking place in virology at present indicate that soon the clinician will not need to rely on clinical criteria alone to establish a diagnosis. Virus laboratory tests are becoming easier and more rapid and thus of increasing interest to the practising physician.

Summary

The clinical features of seventeen cases of aseptic meningitis due to Coxsackie-B virus are described. Three of the cases yielded Coxsackie-B virus in the C.S.F.

It did not prove possible, in the individual case, to distinguish between aseptic meningitis caused by Coxsackie-B, poliomyelitis, or "orphan" viruses.

These seventeen cases formed part of a series of ninety-six cases of aseptic meningitis diagnosed as "non-paralytic poliomyelitis" and studied at the Hospital for Sick Children, Toronto, in 1950–55. Therefore it seems that about 20% of cases of aseptic meningitis in Ontario are caused by Coxsackie-B virus.

We wish to thank the physicians attending the Hospital for Sick Children for allowing us to study their patients, and the previous research fellows whose records made this study possible: Dr. Ross Johnson, Dr. Anne Peach, and Dr. W. J. Fujiwara.

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THYMECTOMY DURING RESPIRATORY FAILURE

IN A CASE OF MYOPATHY WITH MYASTHENIA GRAVIS

S. G. GRIFFIN
M.B. Lpool, F.R.C.S.
THORACIC SURGEON, NORTH REGIONAL CHEST SURGERY CENTRE (SUNDERLAND AREA) AND SEAHAM HALL HOSPITAL, CO. DURHAM

F. J. NATTRASS
M.D. Durh., F.R.C.P.
PROFESSOR OF MEDICINE IN THE UNIVERSITY OF DURHAM

E. A. PASK
O.B.E., M.A., M.D. Camb., F.F.A.R.C.S.
PROFESSOR OF ANÆSTHETICS IN THE UNIVERSITY OF DURHAM

THE patient described here presented an unusual myopathic picture which, at the age of 35, was complicated by severe myasthenia, including virtually complete respiratory failure.

Case-report

A boy, aged 15, was first attended by Dr. C. N. Armstrong. He had been well until the age of 14; he could run, jump, and play games as well as other boys, but at this age he began to have difficulty in holding his arms above his head during physical training. This weakness increased, and soon afterwards he noticed that his left leg seemed to be weak; it would often give way, causing him to fall. Once on the floor, he found it difficult to get up again; he also found difficulty in climbing stairs.

Dr. Armstrong found weakness of pelvic and shoulder-girdle muscles; he diagnosed muscular dystrophy and advised treatment with glycine. This remedy appeared to produce considerable improvement. The patient became able to go upstairs much more easily and tended to fall less frequently. He took glycine for two years and insists that during this period slow, though progressive, improvement took place. He then stopped treatment, but nevertheless improvement continued, and a year later he seemed perfectly normal; he could run upstairs, and his arms seemed to have regained normal power. He remained well for about six years during which he worked as a labourer, but then his muscular trouble gradually returned. As before, it began with weakness in the arms, and difficulty in lifting heavy objects; the arms tired easily. Shortly afterwards difficulty in climbing stairs returned. Weakness of the arms and legs increased, and he had to give up heavy work. He was examined by Dr. J. N. Walton in July, 1951. At no time had he had pain in his limbs, difficulty in swallowing, or weakness of his neck, but his condition was always much worse in cold weather. The cold seemed to make his muscles stiff and made his fingers go white and dead. He had also experienced slow, progressive deafness for ten years. He had one sister, aged 23, who was well; there was no history of muscular disease in the family.

Examination

On examination in July, 1951, he was intelligent, cheerful, and coöperative. He walked with a distinct increase in the lumbar lordosis but did not waddle. He could walk quite quickly but was compelled to use his hands in climbing stairs and could only rise from the floor by pushing his knees with his hands. He had definite slight bilateral ptosis, and his face was rather elongated, but no distinct weakness of the facial muscles was found. He showed signs of bilateral nerve deafness with no evidence of any lesion in the middle ear. The other cranial nerves were normal. There were weakness and wasting of posterior cervical muscles, sternomastoids, trapezii, rhomboids, serrati, pectorals, spinati, latissimi, teres major, deltoids, biceps, triceps, brachioradiales, and the extensors of the wrist and fingers. The power in the wrist and finger flexors was good. The tendon reflexes were present symmetrically but somewhat depressed. The abdominal reflexes were present, but there was some weakness of lower abdominal muscles and of the posterior spinal group. The legs showed wasting and weakness of the glutei maximi, adductors, and hamstrings, but the quadriceps were quite strong, and the muscles below the knee were normal.

Electromyography

An electromyogram was recorded from the left quadriceps, right biceps, and right pectoralis major; in each muscle there was no spontaneous activity, and on volition a sustained but highly polyphasic interference pattern was obtained. Analysis of the record with the audiofrequency spectrometer revealed a shift to the right of the dominant frequency. The pattern was thus characteristic of a myopathy as distinct from a neuropathy.

Muscle Biopsy

A specimen was taken from the left triceps on Nov. 18, 1951, and a portion of overlying skin was also removed. Dr. R. O. K. Schade reported that the muscle showed some atrophic fibres, but there was no proliferation of sarcolemmal nuclei or any cellular infiltration. The epidermis was atrophied and the dermis thickened, with swelling of its collagen fibres. The appearances were not those of dermatomyositis, but no definite diagnosis could be made. We now consider these to be mild myopathic changes.

Treatment and Progress

The patient, seen again on March 19, 1952, showed little change. Treatment with α-tocopherol ('Ephynal,' Roche), 50 mg. t.d.s. was begun. He returned on Sept. 23, 1952, walking more briskly than before. Three weeks after his previous attendance he had stopped taking the ephynal because it did not appear to be doing him any good. A friend of his who had asthma had given him an ephedrine tablet to take on a day when he had a cold and was feeling particularly weak; this produced striking improvement in muscular power. His general practitioner had then given him ephedrine three times a day ever since. These tablets had produced a sustained and dramatic improvement in his condition; within two days he was walking very much better, and soon afterwards he could run upstairs. On examination the muscular wasting was unchanged, but there was an undoubted improvement in muscular power; he could hold his arms above his head without tiring, rise from the floor, and run upstairs without assistance. Intramuscular neostigmine 1·25 mg. produced no objective change in muscular power.

Three years passed in which this improvement was maintained and he did his usual work as a clerk. Then in June, 1955, he returned to the outpatient department with the story of five months' increasing weakness of all limb and trunk muscles, together with weakness of jaw muscles causing difficulty in eating. There was no regurgitation of food but some difficulty in swallowing. These symptoms were always greatly improved by rest, becoming worse as the day advanced and increased by exertion, cold, or emotional excitement.

Admission to Hospital

During the next week or two he became much worse and was admitted to hospital. He then walked with difficulty and with a waddling gait; indeed he could hardly stand. On examination his jaw was dropped, causing great difficulty in feeding and talking. There was probably no weakness of the facial muscles, but his expression was altered by the sagging jaw. The distribution and degree of muscular wasting were essentially unaltered, but weakness was everywhere greatly increased. There was, as before, a general depression of the tendon reflexes; sensation of all types was normal. His general condition was good, and nothing abnormal was found in heart, lungs, or abdomen.

Treatment and Progress

Neostigmine 15 mg. by mouth produced a temporary increase of muscular power, and he was given 15 mg. four times daily in addition to ephedrine gr. $^1/_2$ three times daily (his usual dose). He remained about the same for a week, with only transient improvement after the neostigmine, and the dose was then increased to 30 mg. four times daily. Now, however, weakness increased alarmingly day by day, but respiration was unaffected. With the fear of a respiratory crisis and in the belief that the need was for more neostigmine, the dosage of this was pushed up day by day during the next week till he was receiving 1 mg. intramuscularly each morning and 420 mg. orally throughout the remaining twenty-four hours. Ephedrine gr. $1^1/_2$ daily was continued, and two doses of atropine sulphate gr. $^1/_{120}$ daily were sufficient to prevent

serious colic. An emergency thymectomy was under consideration, when at this time he abruptly developed difficulty in breathing; this appeared about 6 P.M. and by 7.15 P.M. the breathing was mainly diaphragmatic. He could still swallow and could hold up his jaw to enable him to talk. At 8.15 P.M. his breathing was only diaphragmatic and gasping.

Respiration stopped rather suddenly at 8.30 P.M. The senior duty anæsthetist was called urgently and, finding the patient unconscious, apnœic, deeply cyanosed, and apparently pulseless, started mouth-to-mouth artificial respiration, at the same time sending for endotracheal equipment with oxygen.

Intermittent Positive-pressure Respiration

Soon an endotracheal tube was inserted, and manual intermittent positive-pressure ventilation was started. Within two hours an intermittent pressure respirator with facilities for "patient-triggered" operation was in use, and this was continued for the next forty-four days. Facilities for negative pressure during exhalation are available on this respirator, but they were used only temporarily during a period of circulatory collapse on the twenty-seventh day after respiratory arrest. The respiratory gases were air slightly enriched with oxygen. The mixture, which was produced by an oxygen injector, contained about 35% of oxygen. The gas mixture was humidified to about 85% saturation at room-temperature by simple means. There were facilities for humidification to saturation at body-temperature, but it was not considered necessary to bring them into use.

This patient had some breathing power except for the first two days and immediately after his operation. His breathing power, though quite insufficient to maintain adequate ventilation, was enough to "trigger" the respirator. Thus, almost throughout the period of artificial respiration, his pulmonary ventilation remained under the control of his own nervous system, and the respirator supplied the necessary energy on demand. We found this very helpful, for there was never evidence of respiratory acidosis or alkalosis while the respirator was in use.

Once the initial emergency had been overcome, neostigmine was stopped in the hope that spontaneous respiration might return. Twelve hours later this happened but the respiratory power was so feeble that, after two minutes' spontaneous respiration, the patient became very distressed. He had recovered consciousness, and we were relieved to find him mentally clear. After a further two days there was still no significant spontaneous respiration, and under general anæsthesia a tracheostomy was done by Mr. F. McGuckin, and a cuffed tracheostomy tube was inserted to replace the endotracheal tube.

Diet

The patient had great difficulty in swallowing; so he was fed through a stomach-tube with the following mixture:

Casilan	4 oz.
Eggs..	2
Milk	40 oz.
Sugar	4 oz.
Orange-juice	6 oz.
Butter	2 oz.
'Marmite'	1 teaspoonful
Halibut-liver oil	10 minims
Ferri et ammon cit. ..	gr. 90

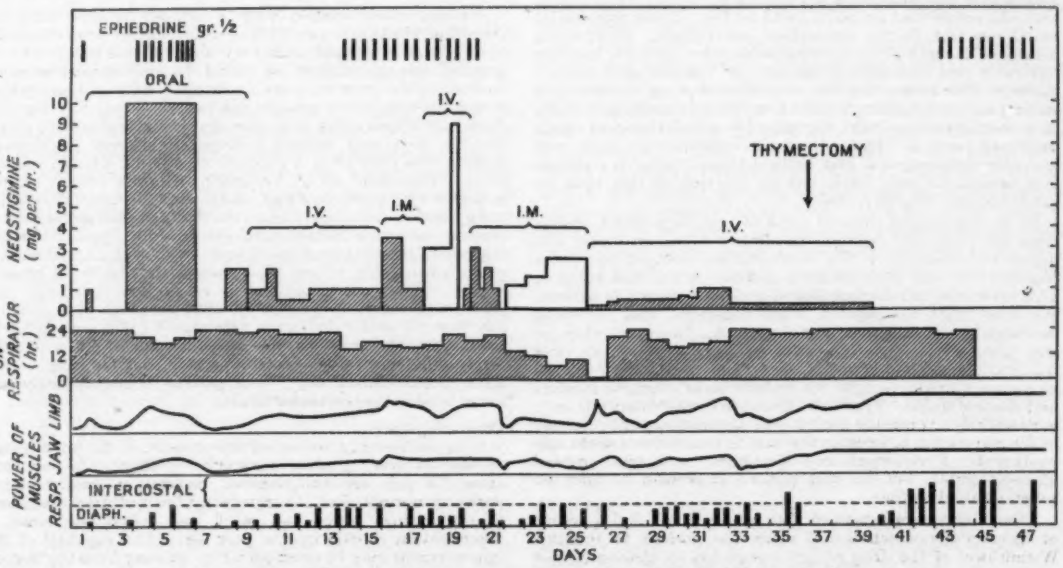
He also received water if he became thirsty. In addition a slow intravenous saline drip was maintained, particularly as a means whereby intravenous medication could be given. The only detectable electrolyte abnormality was a slight fall of the serum-potassium level to 3·1 m.eq per litre about a week after the crisis. This was soon corrected by adding potassium chloride to the intake.

About three weeks after the onset of the crisis the patient developed a confusional state, and for this reason a daily intramuscular supplement of vitamin-B complex was given. Ascorbic acid 100 mg. a day was also added because it was felt that the 60 mg. contained in the food mixture might be insufficient. These supplements were continued until the patient had recovered sufficiently to take a normal diet.

Progress

The accompanying figure presents the important features of the case. The time "on respirator" is reasonably accurate but does not show the length of the periods of spontaneous respiration that the patient could tolerate. Except for days 24–26 these periods did not exceed thirty minutes at a time, and they were usually much less. The power of the respiratory and other muscles was necessarily estimated subjectively, and it must be remembered that more than twenty persons wrote the clinical notes from time to time.

The general course of the treatment was stormy. Suction clearance of the respiratory passages was often necessary; the lungs often partially collapsed. Respiratory obstruction, sometimes complete and requiring urgent treatment, including bronchoscopy, was not unusual. In fact it proved necessary to have a doctor in continual attendance, and more than twenty doctors shared this duty. Nursing difficulties were increased by the frequent and disorderly action of the bowels, perhaps due to the use of antibiotics and the difficulty of maintaining the correct balance of neostigmine and atropine. All these difficulties were increased because, on account of the tracheostomy, the patient could not speak and was too weak to write. The nursing care was devoted and outstand-



Treatment and progress on intermittent positive-pressure respiration and neostigmine.

ingly skilful. Frequent postural changes and physiotherapy were practised throughout.

On the third day neostigmine 0·2 mg. was injected into the left brachial artery as a test. There was a striking increase in the strength of the muscles of the forearm, and we therefore felt confident that the patient had a weakness of skeletal muscles which was responsive to neostigmine.

Accordingly treatment with oral neostigmine was started, and, on this occasion only, responsibility for the treatment was divided so that one of us sought to administer the dose of neostigmine which would allow maximal strength in the skeletal muscles, while another " took care " of the respiration. Despite a considerable return of skeletal muscle power respiration remained very poor. Neostigmine was then stopped and was not started again until we had secured supplies of ' Tensilon ' (3-hydroxyphenyldimethylammonium bromide) through the courtesy of Messrs. Roche Products Ltd., and by the generosity of several anæsthetists in various parts of the country who gave us of their meagre supplies. On the ninth day intravenous neostigmine was started, intermittent doses of tensilon being used to test whether the dosage of the neostigmine was adequate or insufficient. On this basis considerable amounts of neostigmine were given because the tensilon tests were always positive, showing an apparent improvement in skeletal muscle strength but usually without much effect on the respiration.

As the weeks passed, the strain on the patient's morale became even greater. He developed fixed convictions about his treatment, and this made it extremely difficult to interpret his response to tensilon injections, even though dummy injections of saline solution were interspersed with them.

We made frequent attempts to encourage the patient to breathe spontaneously (see figure). During these attempts at spontaneous breathing the pattern of events was usually similar.

He would breathe for a few moments fairly calmly, though respiration was always paradoxical. Then he would become agitated, demanding the respirator, and his breathing became rapid and jerky. It seemed clear that his weak respiratory muscles were not being used to their best advantage. Cyanosis did not appear, for we enriched his inspired air with oxygen; but, if one persisted in the attempt to maintain spontaneous respiration, profuse sweating of the face and hands, rising blood-pressure, slowing of the pulse-rate, and facial twitchings would follow. Soon afterwards the patient would become unconscious, if the attempt were persisted in.

A particularly alarming incident occurred on the twenty-sixth day. With difficulty the patient had breathed all day, and his condition seemed fair, though respiration was always paradoxical. Probably an incident of relative respiratory obstruction precipitated a very sudden circulatory collapse, with the result that no pulse could be felt. There were facial twitchings and, finally, generalised convulsions. Restorative measures, including blood-transfusion, were applied, and the respirator was immediately started. It was not until twenty minutes after re-starting the respirator that we obtained an end-expiratory gas sample, but even then it contained $7^1/_2$% of carbon dioxide. Next morning his circulation was much improved and he had recovered consciousness but was violently agitated and had hallucinations. Heavy sedation was needed for two days, but at the end of this time he again became mentally clear.

In an attempt to unravel some of our perplexities arising from the equivocal reactions natural to a patient under this degree of stress, on a few occasions we changed the gases supplied by the respirator to nitrous oxide and oxygen. This produced unconsciousness with no distress to the patient. We knew that the patient, when conscious, was becoming emotionally dependent on the respirator. However, when he was unconscious due to nitrous oxide, his respiration was still inadequate and paradoxical. There was some response to carbon dioxide, to light concentrations of ether, to lobeline and amphetamine. These all stimulated respiration but only very slightly. When the patient was unconscious, the response of the respiration to neostigmine and to tensilon was slight and equivocal. Pyridostigmine (' Mestinon ') was tried instead of neostigmine, but for this patient it seemed to offer no substantial advantage.

After four weeks it seemed that we could not find a dosage of neostigmine which would allow the patient to breathe. Withdrawal of the drug or low dosage led to distressing jaw and muscle weakness; and, though usually this deterioration of skeletal muscle power seemed to be accompanied by improved breathing, the breathing was never nearly enough.

Thymectomy

The question of thymectomy had been discussed ten days previously, but after careful consideration further medical measures had been decided on. Against surgery were the state of myasthenic crisis and the infection in the neck round the tracheostomy site, this latter making impossible the usual approach to the thymus. Now, however, thymectomy was considered as a last resort. The patient's general condition was poor. There was evidence of severe pulmonary infection and the tracheostomy wound was discharging pus, making the opening of the mediastinum through the neck apparently indefensible. However, despite these contra-indications and with the appropriate antibiotic cover for the known infection, it was decided to remove the thymus through the left pleural cavity. It was felt that the breathing difficulty, so much aggravated by an open pleura in these cases, would be overcome by adequate pleural drainage and the mechanical control already in operation. On the thirty-sixth day, under nitrous oxide and oxygen and pethidine anæsthesia, thymectomy was done.

Operation

A left thoracotomy, after resection of the 5th rib, revealed a free pleura and, after the lung had been retracted posteriorly, a moderately large thymus showing through the mediastinal pleura overlying the aortic arch. There was no other obvious abnormality. The mediastinum was opened anteriorly to the phrenic nerve, and the thymus was dissected from in front of the large vessels. It had a central body with 2 upper and 2 lower prolongations or poles. The thymic veins going to the innominate vein and the vessels in the fibrous prolongation from both upper poles were tied, after dissection up into the neck, without encountering the cervical infection. Some small vessels from the internal mammary artery were tied, and the H-shaped thymus was removed. Subsequent histological examination showed normal thymic tissue with normal involutionary changes, in a gland weighing 15 g. A Malecot catheter with siphon drainage was placed in the 8th space posterolaterally, and the wound was closed in layers.

Postoperative Treatment and Course

Postoperatively the antibiotics were continued systemically. The drainage tube was removed on the third postoperative day, and on the seventh and sixteenth postoperative days 11 oz. and 18 oz. of bloodstained fluid were removed by aspiration from the left side of the chest. Both specimens were sterile on culture. No difficulty was experienced in maintaining full lung expansion and adequate oxygenation by bronchial aspiration through the tracheostomy and the continued use of the mechanical respirator.

Because there seemed only a slender chance that the operation would give benefit, the situation had been explained briefly to the patient and very fully to his relations. A promise was given that he would be spared postoperative distress to the greatest possible extent. After the operation, therefore, respiration was maintained automatically for four days, and liberal doses of opiates and barbiturates were given. On the first and second postoperative days intravenous feeding was used with a mixture of ethanol 44 ml., glucose 50 g., ' Casydrol ' 30 g., potassium chloride 0·8 g., sodium lactate 0·8 g., aneurine 2 mg., nicotinamide 10 mg., riboflavine 2 mg., and pyridoxine 10 mg. On the fifth postoperative day consciousness was allowed to return fully, and " patient-triggered " operation of the respirator began. On the sixth postoperative day a brief trial showed that he could breathe easily, but we were anxious to retain his confidence and little was attempted. It was not until the ninth postoperative day that the senior doctors in attendance could give sufficient continuous attention to the patient to warrant a lengthy test. The respirator was stopped on the morning of the ninth postoperative day. The patient breathed easily and never needed the respirator again.

Later Progress

It is unnecessary to record the details of the later phases of this patient's gradual recovery. Suffice it to say that, since its full re-establishment, respiration has remained perfectly normal, and the myopathy has returned essentially to its original state—i.e., as it was before the onset of deterioration a little over a year ago. The rapidity of this improvement may be exemplified by quoting from the nursing notes sixteen days after operation: he " has been sitting up

tidying his locker !! " He began to get up on the twentieth postoperative day. He has now (May, 1956) been back at work as a clerk for four months his sole medication being ephedrine gr. $^1/_2$ three times daily.

These are the highlights and there were many postoperative anxieties. Of chief interest is to try to assess the postoperative reaction to neostigmine. This was used from time to time in moderate doses (not more than 75 mg. in a day); but, though slight temporary improvement in jaw and limbs usually followed a dose, at the same time the patient tended to feel short of breath, and on the whole the effect was deleterious.

The type of myopathy in this patient differs from any of the classical types and can only be placed in the small group of " myasthenic myopathy " (Walton and Nattrass 1954). The distribution of muscular weakness and wasting is nearest to the limb-girdle (or Erb) type (Walton and Nattrass 1954).

Recent examination reveals slight ptosis, more on the right side than on the left, and diplopia on extreme upward and downward gaze, the right eye moving better than the left. These findings indicate ocular myopathy.

Discussion

There seem to be three possible causes for the failure of breathing in this patient :

(1) An exacerbation of myasthenia gravis occurred suddenly and was not matched by a sufficient increase in the dose of neostigmine.

(2) The patient, in some unexplained way, became temporarily insensitive to the usual antimyasthenic drugs.

(3) The respiratory arrest was in some way associated with the action of neostigmine in a dosage which was excessive for this particular patient.

None of the possibilities can be ruled out, but the first seems unlikely. Despite the positive responses to intra-arterial neostigmine and to intravenous tensilon, additional neostigmine, while improving the power of skeletal muscle, never seemed to improve respiration. Indeed our impression was always that breathing became worse on high dosage of neostigmine.

As regards the third suggestion, the possibility of producing neuromuscular blockade, probably of the depolarising type, with neostigmine has been recognised for some time (Wilson et al. 1952), and clinical cases of this effect have been described by Tether (1955) and Osserman and Kaplan (1953). Rowland et al. (1955) report the production of weakness in myasthenic patients by large dosage of intravenous neostigmine.

Several of these workers note that, in the presence of adequate atropine, the muscarinic symptoms of the cholinergic crisis may be wholly or partly suppressed ; only muscular weakness may be manifest, and this may particularly affect breathing.

Though our patient was receiving large doses of neostigmine when his respiration ceased, they were not so great as the doses associated with cholinergic crisis in most other reports. Furthermore, neostigmine was withdrawn completely for three days and maintained at a low level for ten days, but respiration remained very unsatisfactory. Nevertheless, there was always the impression that the more neostigmine the patient received the more imperfect became his respiration. It has to be recognised also that eventual recovery followed two important events : (1) thymectomy and (2) the virtually complete withdrawal of neostigmine for twelve days, a period longer than that of any previous withdrawal.

One feels bound to ask whether neostigmine could have an action on respiration which is more prolonged than any we normally associate with the drug. Many mechanisms might be considered, but one possibility might be that, in certain persons after prolonged administration, neostigmine might reach a compartment of the body-fluid from which it is normally excluded and, having entered, might only slowly be eliminated. The so-called " blood-brain " barrier comes to mind ; and, though there is no direct evidence at all for the hypothesis, it is made a little less impertinent by the recent work of Eccles et al. (1956), who, investigating the effect of drugs upon the activity of Renshaw cells in the spinal cord, found that intra-arterial neostigmine did not normally affect them, though intra-arterial eserine and tetraethyl pyrophosphate did, causing considerable prolongation of the discharge evoked by an antidromic volley. Neostigmine apparently did not normally reach these cells of the central nervous system when injected intra-arterially, for it was active when injected by micro-pipette directly into the neighbourhood of the Renshaw cell under observation. However, in two of eight Renshaw cells examined in this way, intra-arterial neostigmine was observed to have an effect comparable to that of eserine, being perhaps able to penetrate the " blood-brain " barrier in these instances.

Any suggestion that the cause of insufficient respiration in our patient was an influence acting centrally rather than peripherally must recognise that the patient's ability to control his respiration seemed to be intact. With the aid of the " patient-triggered " respirator his blood oxygenation and acid/alkali balance remained normal. Furthermore the qualitative response of his breath-controlling mechanisms to respiratory stimulants seemed normal.

The practical outcome of this reflection is, however, that, if we were dealing with another myasthenic patient in whom respiratory paralysis occurred while large and increasing doses of neostigmine were being given, we would be inclined to establish satisfactory artificial respiration and then to withdraw the neostigmine for a week or so rather than for the much shorter periods we would hitherto have considered adequate for its complete elimination.

It has recently been suggested that, when large doses of neostigmine seem to be indicated, a considerable proportion of it should be given by intramuscular injection because there is uncertainty about the rate and regularity of absorption of neostigmine from the intestine (*Lancet* 1956). It also appears prudent to be at some pains to keep the concomitant dose of atropine as low as possible, for a sudden increase in muscarinic symptoms might then give warning of accelerated absorption. The postulated effect of excessive neostigmine in producing muscular weakness is distinct from its muscarinic effect, but a sudden acceleration of absorption might presumably lead to both effects.

A single case can add little or nothing to the assessment of the importance of thymectomy in this confusing disease. We do not think that there are many recorded instances of thymectomy during a crisis when the patient was in respiratory failure, for the operation in such circumstances must be considered very hazardous. However, given experienced surgery, devoted nursing, and a satisfactory means for maintaining respiration, it evidently is possible to succeed. As a matter of history, satisfactory breathing returned after the operation, and in similar circumstances, when every attempt to find the correct dosage of an antimyasthenic drug had failed, we would again favour the attempt at thymectomy.

Summary

A case of atypical myasthenia gravis is described in which respiratory failure occurred.

Artificial respiration was maintained for several weeks, but it proved impossible to secure the return of breathing by the use of the usual antimyasthenic drugs.

Eventually thymectomy was done while the patient was still in respiratory failure, and after the operation full respiratory power returned.

The patient recovered to a condition as good as, or slightly better than, that which prevailed before the crisis, and he no longer requires neostigmine.

It is impossible to mention by name all the doctors who worked for this patient; more than twenty were concerned. Messrs. Roche Products Ltd., Medical Division, not only helped us by providing 'Tensilon' but also furnished much information about myasthenic and cholinergic crisis.

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A FATAL CASE OF GLANDULAR FEVER

N. K. SHINTON
M.B. Birm., M.R.C.P.

SENIOR REGISTRAR IN CLINICAL PATHOLOGY, QUEEN ELIZABETH HOSPITAL, BIRMINGHAM

C. F. HAWKINS
M.D. Lond., F.R.C.P.

CONSULTANT PHYSICIAN TO THE UNITED BIRMINGHAM HOSPITALS AND MID-WORCESTERSHIRE GROUP; LECTURER IN CLINICAL MEDICINE IN THE UNIVERSITY OF BIRMINGHAM

GLANDULAR fever, remarks Tidy (1950), began its clinical life as a simple harmless adenitis. It was first described by Pfeiffer (1889), and since then various forms of it have been recognised, such as the anginose type (Schultz 1922), which mimics diphtheria in that a membrane appears in the throat, and the prolonged febrile forms with little or late glandular enlargement that may simulate typhoid or other fevers and were recognised by Tidy (1931) during an epidemic of glandular fever in England in 1930.

The onset of glandular fever with jaundice has become increasingly noticed (Leibowitz 1953), when it may appear identical with infective hepatitis.

A wide variety of neurological manifestations of glandular fever have been reported, ranging from encephalitis to affections of the spinal cord and cranial and peripheral nerves either separately or in different combinations (Epstein and Dameshek 1931, Johansen 1931, Geliebter 1946, Schneider and Michelson 1947); and sometimes a benign lymphocytic meningitis may be the first indication of glandular fever.

In spite of the alarming nature of many of the symptoms it is generally accepted that glandular fever is benign, complete recovery being invariable though possibly somewhat delayed in some patients. Death is rare, and Tidy (1950) had never seen a case which did not recover completely. It therefore seems worth while to publish the following fatal case.

Case-report

A boy, aged 17, of normal physique and previously in perfect health, developed a sore throat and pyrexia in early November, 1955. His high temperature persisted, and he was treated with penicillin and streptomycin. After a few days a membrane appeared on his tonsils and posterior pharyngeal wall, and his cervical glands were enlarged. A throat swab showed no microscopical evidence of Vincent's infection, and cultures from it yielded a heavy growth of α-hæmolytic streptococci; no *Corynebacterium diphtheriæ* or β-hæmolytic streptococci were isolated. At the end of ten days the pyrexia had subsided, but the boy appeared very toxic and was vomiting intermittently. There was then gross lymphadenopathy involving the cervical, supraclavicular, epitrochlear, and inguinal groups, and the spleen was palpable. Blood-films then taken were reported by the hæmatologist (Dr. M. J. Meynell) as showing severe neutropenia and atypical mononuclear cells similar to those seen in glandular fever. The Paul-Bunnell test, after absorption of the serum with guineapig kidney, was positive to a titre of 1 in 512. After a temporary improvement the patient suddenly relapsed and became delirious, with further pyrexia. He was admitted to hospital on Nov. 25.

On admission he appeared very toxic, with a temperature of 102·4°F, and was sweating profusely; respirations 35 a minute, pulse-rate 120, blood-pressure 105/50 mm. Hg. He was slightly and intermittently delirious; his tongue was dry and furred; the grey membrane was still present in his throat but smaller, together with œdema and injection of the uvula and soft palate. The lymphadenopathy was unchanged. The spleen was larger but only palpable about 1 inch below the costal margin. There was definite neck rigidity, and a positive Kernig's sign was elicited; no other abnormal signs were detected in the central nervous system.

Lumbar puncture showed clear fluid under a normal pressure of 160 mm., with normal dynamics, less than 1 mononuclear cell per c.mm., normal biochemistry (protein 25 mg. per 100 ml., sugar 57 mg. per 100 ml., sodium chloride 682 mg. per 100 ml., and Pandy and Nonne-Apelt tests for globulin both negative).

Examination of the blood showed 3200 leucocytes per c.mm. (neutrophil polymorphs 2140, lymphocytes 740, monocytes 160, plasma cells 130, and atypical mononuclears 30 per c.mm.). Hæmoglobin 10·8 g. per 100 ml. A further differential Paul-Bunnell test was positive to a titre of 1 in 512.

Treatment and progress.—The pyrexia persisted over the next three days. Daily blood-cultures were negative. The boy was treated with intramuscular tetracycline 100 mg. four-hourly for forty-eight hours, but his temperature remained 101–102°F. His blood-urea level rose to 205 mg. per 100 ml. in spite of a reasonable output of urine (43–115 oz. a day). He was infused with 5% glucose and *N*/5 saline solution two pints alternating with one pint of Hartmann's solution at a rate of one pint in three hours. His blood-pressure was maintained at about 130/90 mm. Hg. His urine was of satisfactory concentration and contained a trace of albumin, with hyaline casts visible on microscopy. Despite treatment he remained very toxic and intermittently delirious and had signs of meningism with occasional vomiting. He died three days after admission to hospital.

Necropsy Findings

All the deep cervical lymph-nodes were much enlarged and matted together, showing on section areas of hæmorrhage and necrosis. The hepatic nodes were similar in appearance, the mesenteric and para-aortic nodes enlarged but discrete, and the mediastinal nodes normal. The thymus (20 g.) was similar on section to the deep cervical and hepatic lymph-nodes. The tonsils were enlarged and necrotic, and ulceration of the pharynx extended into the piriform fossa. The larynx, trachea, and bronchi appeared normal. The lungs were moderately congested and œdematous, with perivascular and peribronchial "cuffing" by lymphocytes, and with a few

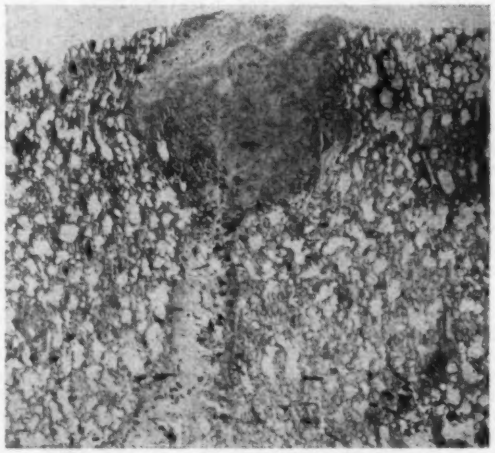

Fig. 1—Section of lung showing nodule of lymphoid tissue (×5).

nodules of lymphoid tissue showing areas of hæmorrhage and necrosis similar to those seen in the lymph-nodes (fig. 1). The liver (1970 g.) had round contours and, on section, white narrow bands of lymphoid tissue along the portal tracts. The spleen (820 g.) was soft and very friable; on section the normal architecture had disappeared, there being no evidence of the malpighian bodies; and pulp was soft but contained numerous white firm areas of necrotic tissue up to 1 cm. in diameter (fig. 2). There was a horseshoe kidney (420 g.) with two normal ureters, leaving a normal renal pelvis on either side. On section the renal parenchyma was normal. The pancreas and suprarenal, thyroid, and pituitary glands showed no macroscopic abnormality. Atypical mononuclear cells were seen in the lymphoid tissue of the deep cervical and hepatic lymph-nodes, spleen, tonsils, liver, thymus, suprarenals, and in the bone-marrow. Detailed examination of the brain, spinal cord, peripheral nerves, and meninges showed no round-cell infiltration or other significant changes.

Fig. 2—Cut surface of spleen showing areas of necrosis.

Discussion

The clinical picture of a tonsillar membrane resembling that of diphtheria in a patient with pyrexia, generalised enlargement of the lymph-glands, and splenomegaly strongly suggested glandular fever. This was confirmed by the presence of atypical mononuclear cells in films of the peripheral blood, and by a strongly positive Paul-Bunnell test, after the serum had been absorbed by guineapig kidney, a finding that is regarded as specific for glandular fever by Davidsohn et al. (1951). Moreover there was a small epidemic of glandular fever at the time and a boy aged 14, a friend of our patient, was also severely ill with the anginose type of glandular fever and had a similar membrane in his throat.

The necropsy findings are unusual in the extent of necrosis found in the lymph-nodes and other lymphoid tissue and spleen. In this respect the histological appearances resemble a malignant reticulosis. The atypical mononuclear cell seen in the lymph-nodes, spleen, and other tissues of the body was similar to that described and illustrated by Custer and Smith (1948) and Sharp (1950), who regard this cell as the same as that seen in the peripheral blood in glandular fever; but it is difficult to compare cells stained after fixation with cells from smear preparations, even when the same stain is used. The extent of tissues involved by infiltration with lymphocytes and atypical mononuclear cells demonstrates the pathological basis of the protean clinical picture. It is surprising that in such a severe case the central nervous system was not involved.

The cause of death must be assumed to be toxæmia, the toxin arising either from an infecting organism or from a breakdown product of the tissue necrosis. The raised blood-urea level was possibly of the latter origin, there being no extrarenal cause and no histological evidence of renal damage. The infiltration of the suprarenal medulla did not give rise to clinical symptoms, there being no evidence of hypotension. There was no improvement after penicillin, streptomycin, or tetracycline therapy.

REPORTED CAUSES OF DEATH IN 21 CASES OF GLANDULAR FEVER

Reference	Cause of death
Du Bois (1930)	Empyema
Elmenhoff-Nielsen (1935) ..	Lobar pneumonia
Thomsen and Vimtrup (1939)	Pneumococcal septicæmia
,,	Central respiratory paralysis
Andersen (1939)	Hæmorrhage from ruptured spleen
Jersild (1942)	"Myocarditis"
Ziegler (1944)	Hæmorrhage from ruptured spleen
Fisher (1946)	,,
,,	,,
Custer and Smith (1948) ..	,,
,, ..	,,
,, ..	Pulmonary embolism following operation for ruptured spleen
,, ..	Lower-nephron syndrome following operation for ruptured spleen
,, ..	Peripheral respiratory paralysis (Guillain-Barré)
,, ..	,,
,, ..	Nasopharyngeal hæmorrhage
,, ..	Laryngeal œdema
Dolgopol and Husson (1949)	Central respiratory paralysis
Ainley (1949)	Intestinal hæmorrhage complicating central zonal necrosis of liver
Sharp (1950)	Sudden pneumothorax
Kass and Robbins (1950) ..	Hæmorrhage from ruptured spleen

Published reports include 26 cases with full necropsy findings. Korsakoff's (1905) patient had a streptococcal tonsillitis with cervical adenitis complicated by acute nephritis. In 2 cases of Haken (1927) diphtheria bacilli were recovered, and a 3rd case of his is also questionable, because of the absence of serological tests. One patient studied by Custer and Smith (1948) died in an aeroplane accident. The alleged causes of death in the remaining 21 cases are shown in the accompanying table. In both cases of death from central respiratory failure degenerative changes were found in the medulla oblongata. In the two cases of peripheral respiratory failure mononuclear infiltration was seen in the anterior spinal nerve-roots at all levels, the myelin sheaths being swollen and disrupted. In the case reported by Elmenhoff-Nielsen the illness lasted a hundred and thirty days with persistent severe neutropenia.

Summary

A fatal case of glandular fever is described.

An unusual feature of the necropsy was extensive necrosis in the enlarged lymph-nodes and spleen.

We wish to acknowledge the helpful advice given by Prof. J. W. Orr in the preparation of this paper.

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ADRENAL ADENOMATA IN ELDERLY DIABETICS

J. J. DALY
M.B. Camb., M.R.C.P.
REGISTRAR, THE ROYAL HOSPITAL, SHEFFIELD

THE rôle of the endocrine system in diabetes mellitus is as yet uncertain. There is much tentative evidence implicating the adrenal glands.

Recent advances in adrenal physiology led me to make a retrospective search for cases of diabetes mellitus associated with so-called cortical adenomas.

Observations

At the Royal Hospital, Sheffield, 789 necropsies were performed in 1953–55, and adrenal tumours were noted in 31 of these. Their incidence was thus almost 4%, which agrees closely with an estimate by Karsner (1950). All the tumours were benign: they were between 1 cm. and 5 cm. in diameter, situated in the normal cortical substance, and bright yellow. In 2 cases bilateral tumours were found. There were no cortical nodules and in no case was there evidence of adrenal atrophy.

The clinical notes disclosed that 6 of these patients (all of them women) had had diabetes mellitus. During the period of review 30 patients with diabetes had died in the hospital, and 20 of these had come to necropsy. The diagnosis had been established, during initial attendances at the clinic, by means of a fasting blood-sugar estimation or a glucose-tolerance curve.

Table I gives details of the 31 cases in which adrenocortical adenomas were found, and table II of the 20 diabetics who came to necropsy. It will be seen that an adrenal tumour was associated with about 1 in every 4 cases of diabetes. In all the cases section of other endocrine glands revealed little of note.

These 6 patients with adrenal tumours were elderly and obese. Their diabetes, so far as could be measured, was of short duration and mild, being controlled by diet alone or in combination with small doses of insulin. The patients had been admitted to hospital because of vascular disease. 3 had had a leg amputated, and the other 3 had died of coronary thrombosis. None had revealed clinical evidence of other endocrine disorder. There seemed to be no striking clinical difference between these 6 patients and the patients of similar age among the 14 without adenomas. The general impression gained from the necropsy findings was that atherosclerosis was more severe among the former, but their number is small. The predominating renal lesion in most of them appeared to be a combination of arterial degenerative disease and infection. Only 1 case had the features of the Kimmelstiel-Wilson syndrome.

TABLE I—PATIENTS WITH ADRENOCORTICAL ADENOMAS 1953–55

Age (yr.)	Sex	Conditions leading to death
45	F	Hypertension
51	M	Hypertension
79	F	Diabetes and peripheral gangrene
77	F	Diabetes mellitus and coronary thrombosis
60	M	Nephrosclerosis
63	M	Ruptured bladder
60	M	Carcinoma of lung
68	F	Diabetes mellitus and hypertension
62	M	Congestive heart-failure
71	F	Cholecystitis
84	M	Prostatic hypertrophy
67	M	Diverticulitis
74	M	Coronary thrombosis
68	F	Diabetes and peripheral gangrene
59	F	Carcinoma of colon
73	F	Diabetes and peripheral gangrene
72	F	Pulmonary embolus
70	M	Coronary thrombosis
75	F	Cholecystitis
73	M	Carcinoma of bladder
58	M	Hypertension
85	F	Femoral thrombosis
68	M	Carcinoma of lung
76	M	Coronary thrombosis
45	M	Coronary thrombosis
59	M	Carcinoma of lung
70	M	Carcinoma of œsophagus
59	M	Coronary thrombosis
80	F	Pulmonary embolus
66	F	Kimmelstiel-Wilson syndrome
57	M	Endocarditis

Discussion

Patients treated for a long time with either corticotrophin or cortisone occasionally reveal glycosuria (Sprague 1951, Sprague et al. 1951). Decreased renal tubular absorption of glucose may play a part in its production (Bishop and Glyn 1952). In these cases a positive family history of diabetes or previous evidence of disturbed carbohydrate metabolism is usually obtained.

The syndrome of steroid diabetes is now well documented and has been produced experimentally in animals by Ingle et al. (1951). In man it is seen in Cushing's syndrome. The disturbance of carbohydrate metabolism is attributed to an excessive output of glucocorticoids by the adrenal glands, and light has been thrown on the mechanism by Ingle et al. (1945). Probably the main factors are increased gluconeogenesis from protein and decreased peripheral utilisation of glucose. Ingle et al. (1945) compared the pancreatic diabetes of rats with that induced by corticosteroids and concluded that insulin exerted little action in control of the latter. Relative insulin resistance and negative nitrogen balance are features of this syndrome.

TABLE II—DIABETICS WHO CAME TO NECROPSY IN 1953–55

Age (yr.)	Sex	Daily dosage of insulin	Duration of diabetes	Complication leading to death
73*	F	Nil	4 years	Peripheral gangrene
77*	F	10 P.Z.I.	5 years	Coronary thrombosis
66*	F	28 P.Z.I.	5 years	Kimmelstiel-Wilson syndrome
68*	F	28 S.I. ?	?	Coronary thrombosis, peripheral gangrene
79*	F	Nil	4 years	Peripheral gangrene
68*	F	20 P.Z.I.	6 years	Coronary thrombosis, peripheral gangrene
62	M	54 P.Z.I. 40 S.I.	8 years	Coronary thrombosis
52	F	Nil	9 years	Papillitis necroticans
78	F	10 P.Z.I.	20 years	Ruptured aorta
41	M	40 P.Z.I. 20 S.I.	20 years	Pyelonephritis
43	F	64 S. 50 P.Z.I.	13 years	Pulmonary embolus
65	F	Nil	? 4 days	Pyelonephritis
62	F	Nil	1 year	Hypernephroma
73	M	Nil	1 month	Carcinoma of bronchus
72	F	20 P.Z.I. 18 S.I.	17 years	Cerebral hæmorrhage
64	F	Nil	5 years	Bronchopneumonia
64	F	Lente 16	2 years	Leukæmia
19	F	Insulin + ? amount	?	Diabetic coma
69	F	?	?	Coronary thrombosis
44	M	?	?	Coronary thrombosis

* Adrenocortical adenoma present.

Hubble (1954) recorded the case of a girl, aged 13, with diabetes, who exhibited much resistance to insulin. Fluctuating levels of urinary corticosteroids were obtained. Hubble concluded that the insulin resistance was not due to excess adrenocortical function but was related to the growth hormone of the anterior pituitary.

Many cases of endocrine upset in association with hyperplasia or tumour of the adrenals show features of both the adrenogenital syndrome and Cushing's syndrome. The final clinical picture probably depends to some extent on the relative output of androgens and glucocorticoid substances.

Balfour and Sprague (1949) reported Cushing's syndrome in a boy, aged 15, with severe diabetes and abnormal amounts

of 17-hydroxycorticosterone in his urine. He was insulin-resistant and had hyperplasia of the adrenal glands.

A remarkable case was reported by Sprague et al. (1943):

A middle-aged woman with three years' history of diabetes required up to 145 units of insulin daily for control of symptoms. A large adrenal tumour was excised at laparotomy. Eight months later she was well and her glucose-tolerance curve was normal. She had no other endocrine abnormalities, and her family history was negative. No urinary assays were done.

Most reports of adrenocortical function in diabetes show diminished activity.

Wolfe and Paschkis (1952) found a low urinary excretion of formaldehydrogenic steroids in more than half of 42 diabetics. Talbot et al. (1951) found a low urinary excretion of corticosteroids in 4 diabetics. Miller and Mason (1945) also reported low urinary excretion of 17-ketosteroids. Becker (1952) and Becker et al. (1954), however, found increased adrenal activity among patients with retinopathy. Becker (1952) noted at necropsy that the adrenals weighed more in diabetics with Kimmelstiel-Wilson syndrome than in other diabetics.

Increased excretion of corticosteroids has also been recorded in diabetics with these complications. It must be noted, however, that an increased output of hormones influencing carbohydrate metabolism may not be reflected by higher urinary excretion of ketosteroids. The methods used in the above series are difficult to apply and involve losses in extraction. The method introduced by Norymberski (1952) and Norymberski et al. (1953) for estimating the urinary excretion of ketogenic steroids solves some of these problems. Nelson and Samuels (1952) described a method of measuring plasma levels of compound F, but it is not yet practicable as a routine laboratory procedure.

The 30% incidence of benign adenomas among elderly diabetics may be confirmed or refuted by further study of necropsy material. The evidence pointing to the part played by adrenal hormones in carbohydrate metabolism may suggest a causal relationship. Certain similarities between the diabetes seen in later life and the steroid variety do exist. Adrenal tumours in association with diabetes mellitus have been reported. The application of new methods of hormone assay may provide further information.

Summary

A high incidence of adrenal adenomata among elderly diabetics is reported. Its significance is discussed.

I wish to thank Dr. J. L. Edwards for his help and permission to use post-mortem records.

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Reviews of Books

Histological Appearances of Tumours

With a consideration of their histogenesis and certain aspects of their clinical features and behaviour. R. WINSTON EVANS, T.D., B.SC., M.R.C.S., consultant pathologist, United Liverpool Hospitals. Edinburgh: E. & S. Livingstone. 1956. Pp. 773. 90*s*.

THE most difficult problem for the hospital pathologist is to express an opinion on the microscopical appearances of a piece of tissue. He is required not only to give an accurate diagnosis, but also to state the probable origin of the lesion and to forecast the subsequent course of the disease. This book supplies in an interesting and concise form the knowledge needed as a background for diagnosis in a difficult case.

The tissues of the body, subdivided on an embryological basis, are considered in turn as the starting-point of tumours of various systems—connective and skeletal tissues, blood-forming organs, epidermis, and so on. There is an excellent chapter on melanoma, followed by one on tumours of the nerve-sheath (where neurilemmoma is consistently misspelt). Intracranial neoplasms and tumours of the female generative system are omitted, as the author regards these as well covered in special textbooks. The chapters on tumours of the mammary gland and of the endocrine glands are very good. The 989 illustrations are nearly all excellent photomicrographs. The author's hope that these figures will be useful to the pathologist who is discussing a case with a clinical colleague is likely to be realised; but they will be still more useful to the pathologist himself. Stress is laid on the need, in tumour diagnosis, for a good section together with knowledge of the clinical details. (To these requirements might be added the need for an adequate piece of tissue, delivered to the laboratory in proper condition.)

This important book is likely to be widely used.

Therapeutic Use of Artificial Radioisotopes

Editor: PAUL F. HAHN, PH.D., Cancer Research Laboratories, Nashville, Tennessee. New York: John Wiley. London: Chapman & Hall. 1956. Pp. 414. 80*s*.

THIS is a composite work, predominantly American but including also contributions from other countries.

Preliminary chapters on purely physical aspects of radioactivity are followed by 13 chapters on clinical applications, including four excellent contributions from this country on radio-iodine treatment of thyrotoxicosis and thyroid carcinoma, on local treatment of bladder tumours, and on beta and gamma applicators. The chapter on the use of radio-phosphorus gives a distinctly one-sided account of the therapy of leukæmia and polycythæmia, in that only one technique is described, with the implication that all others are worthless; but this impression is partly corrected by the succeeding chapter, which describes the treatment of leukæmia by intravenous radioactive colloids.

In spite of some unevenness in the clinical sections the general standard is high and the book will certainly prove valuable for anyone engaged in these new modes of therapy.

Treatment of Migraine

JOHN R. GRAHAM, M.D., chief, medical service, Faulkner Hospital, Boston. Boston: Little, Brown. London: J. & A. Churchill. 1956. Pp. 149. 28*s*.

THIS is an excellent review by one who clearly has a wide experience of migraine and much sympathy with its sufferers. It is brief, practical, and well balanced.

Although primarily concerned with treatment it devotes a useful chapter to diagnosis, making it clear that "migraine" is not interchangeable with "headache." Treatment is linked rationally to the considerable amount that is now known of the mechanism of the migraine attack, and prophylaxis is discussed similarly. The part that the stresses and strains of everyday life play in precipitating attacks, and the adjustment of ways and aims, are presented in a refreshingly common-sense way.

This book should find its way into the hands of many general practitioners, but its high price may prevent that.

Ulcers of the Legs

P. PIULACHS, M.D., chief professor surgeon, Faculty of Medicine, Barcelona. Springfield, Ill.: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1956. Pp. 574. £5 17*s.* 6*d.*

THIS book is based on Professor Piulachs's monograph in Spanish published in 1950. It is devoted essentially to the physiopathology, diagnosis, and treatment of lower-leg ulceration, on which Professor Piulachs has contributed many original and novel conceptions.

The book represents personal viewpoints rather than standard opinions. Because of this, it is often interesting and stimulating, but it can be recommended only to those with considerable personal experience of vascular surgery. The text is uneven, tortuous, and often ambiguous—faults commonly associated with too literal translation from a romance language.

Management of Life-threatening Poliomyelitis

Copenhagen 1952–1956. With a Survey of Autopsy Findings in 115 Cases. Editor: H. C. A. LASSEN, M.D., professor of epidemiology, University of Copenhagen. Edinburgh and London: E. & S. Livingstone. 1956. Pp. 179. 22*s.* 6*d.*

IN five months in 1952 the Blegdam Hospital in Copenhagen admitted 2241 patients with poliomyelitis, of whom 345 had impaired respiration or swallowing and were therefore in danger of their lives. By brilliant improvisation Professor Lassen and his anæsthetist colleague, Dr. B. Ibsen, saved the situation by introducing artificial respiration by intermittent positive pressure. This book describes the experiences of the large team involved in this tour de force.

Anyone who has not read previous reports of it will find the book fascinating. Others may be disappointed that this work, which claims to deal with the period from 1952 to 1956, tells us so little of developments in the past three years. Further information about the clinical performance of various mechanical respiration pumps would have been welcome. It is surprising to find cuirass respirators considered in the treatment of acute cases, and the failure to distinguish between the capabilities of the cuirass and that of the tank respirator may account for the low opinion the authors appear to have of tank respirators.

This book, though giving an interesting account of many aspects of the 1952 epidemic, does not constitute, as its title might suggest, an up-to-date textbook on life-saving treatment in poliomyelitis.

Studies in Topectomy

Editors: NOLAN D. LEWIS, M.D., CARNEY LANDIS, PH.D., D.SC., H. E. KING, PH.D. New York and London: Grune & Stratton. 1956. Pp. 248. 48*s.*

THIS book comprises a series of studies on the effects in 66 patients of localised excision of two separate areas of frontal-lobe tissue. In 39 cases Brodmann's areas 9 and 10 was excised (the S operation) and in 27 the orbital frontal cortex (the O operation).

On the physiological level the patients showed a little transient instability of autonomic function; and after the S operation, the ability to perceive "autokinesis"—the apparent movement of an observed stationary object—was altered. In psychometric tests and tests designed to study more complex mental function involving mental arithmetic, learning processes, and memory, there was little change; but, in so far as there was any change, O operations had a less adverse effect on intellectual function than S. The methods devised by the Columbia-Greystone frontal-topectomy workers for studying spontaneous activity for a standard time and in a standard situation, both alone and in company, were applied to these patients. A slight increase in activity was noted after operation; the effect of S and O operations seemed to differ according to whether the patients were alone or in company.

The operations were undertaken in the treatment of chronic psychotic disease. The over-all psychiatric results were not impressive—22% of the patients were improved and 14% were sufficiently well for discharge from hospital—but adverse effects on personality were minimal.

This is one of several combined studies of frontal-lobe function from America. They tend to confirm the impression that frontal-lobe function is less readily studied by formal laboratory and hospital observation than by noting general behaviour changes in the flexible environment of the home. Such tests as that of "spontaneous activity" are thus likely to be rewarding: unfortunately the report on this in the present volume is prolix and difficult to follow. In general frontal-lobe studies continue to emphasise that the function of these areas is complex, variegated, and biologically important.

Landmarks in the History of Hygiene

HENRY E. SIGERIST, D.LITT., D.SC., F.R.C.P., research associate in the history of medicine, Yale University. New York and London: Oxford University Press. 1956. Pp. 78. 12*s.* 6*d.*

THE Heath Clark lectures were founded to emphasise the historical, cultural, and philosophical aspect of public health. The lectures reprinted in this volume were given at the London School of Hygiene and Tropical Medicine in 1952 by the doyen of medical historians, a man of immense learning and linguistic ability. They are well worthy of the lecturer and make lively reading for anyone interested in the subject. They deal with two early classics of hygiene, the quest for long life in the Renaissance, Johann Peter Frank, and the changing pattern of medical care. In his preface Dr. Sigerist recaptures the atmosphere of more leisurely days:

"In the summer of 1911—a coronation year—a summer full of sunshine, in a world that did not require passports—I came to London, a Swiss student from the University of Zürich, just twenty years old. I was not enrolled for a degree, but spent an all-too-short summer term here, attending courses. I was not a medical student then, but was studying Oriental languages and literature; and I remember my teachers with affection and gratitude. I sometimes felt guilty towards them, because in most of these courses I was the only student so that they had all the trouble of preparing the course and coming to the School for a single student. I had two Arabic courses with Professor Hirschfeld, in one of which we read a historical book while in the other we studied ancient Arabic poetry, and I was his only student."

You and Your Operation

B. N. BROOKE, M.D., F.R.C.S., department of surgery, Queen Elizabeth Hospital, Birmingham. London: Faber & Faber. 1956. Pp. 80. 7*s.* 6*d.*

HERE is an admirable guide for the patient likely to need or about to have an operation in a hospital. What and whom he may encounter as outpatient, inpatient, subject of operation, and convalescent are set forth in full with functions and *raisons d'être*. The reader gets a glimpse of the surgeon's mind and will know when and of whom to ask questions. A glossary of specialists, one hospital's rules and weekly menus, and National Insurance rules and forms appear in appendices.

Techniques and Procedures of Anesthesia (2nd ed. Oxford: Blackwell Scientific Publications. 1956. Pp. 568. 66*s.*).—So much has happened in anæsthesia since the first edition of this work, by Prof. John Adriani, was published in 1947 that not surprisingly the present volume has increased in size by nearly 200 pages. The book is designed to illustrate fundamental principles for students and practitioners first encountering clinical anæsthesia, and is largely written in tabulated note form. This makes for heavy reading and somewhat dogmatic statements of fact without the opportunity for discussion, and may account for some of the shortcomings in accounts of certain procedures. Used, as is intended, in conjunction with clinical teaching by an experienced anæsthetist it is a useful, though elementary, outline of practical anæsthesia.

Neuropharmacology (New York: Josiah Macy, jun., Foundation. 1956. Pp. 328. $4.25).—The transactions of the second conference on this subject, held by the Macy Foundation during May, 1955, have now been published under the editorship of Dr. Harold A. Abramson.

Mental Health in Public Affairs (London: Oxford University Press. 1956. Pp. 254. 40*s.*).—This subject was chosen as the theme of the fifth International Congress on Mental Health, held at Toronto in 1954. The report of the conference has now appeared under the editorship of William Line and Margery R. King.

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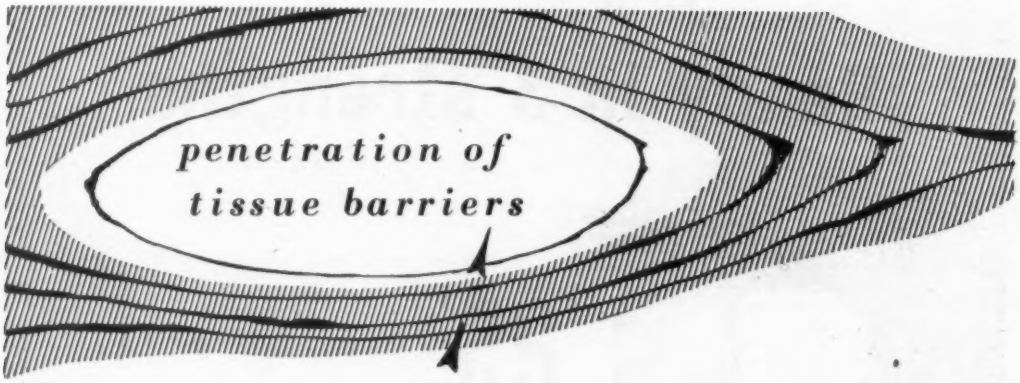

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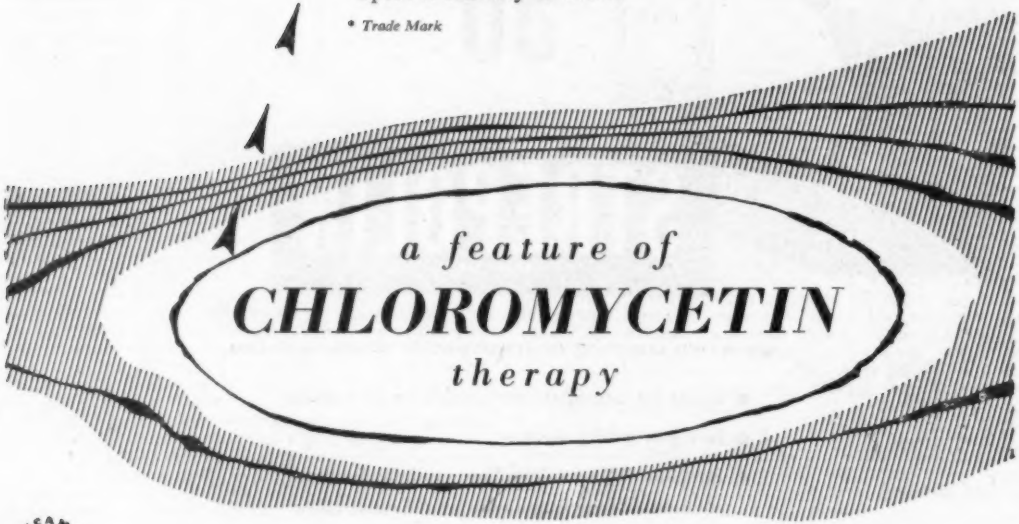

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Megaloblastic Anæmias

FOR the best known of the megaloblastic anæmias, addisonian pernicious anæmia, we have at present a rational explanation. The erythroblast needs vitamin B_{12} (cyanocobalamin) for its proper development; the vitamin B_{12} is in the diet and, in the presence of the intrinsic factor secreted by the glands of the upper part of the human stomach, it is absorbed in the small intestine and passes in the blood-stream to the bone-marrow. In pernicious anæmia the intrinsic factor is no longer secreted, so the vitamin B_{12} passes down the alimentary tract unabsorbed, and without it the erythroblasts show the typical nuclear and cytoplasmic changes that characterise the megaloblast. But pernicious anæmia is now known to be only one of a group of megaloblastic anæmias, and an unexpected finding has been that though some of these non-pernicious megaloblastic anæmias respond to treatment with vitamin B_{12}, many of the patients will respond only to folic acid. For identifying these megaloblastic anæmias, and getting to know something about their causes, new methods have been developed in recent years, and these methods and their results have lately been reviewed by GIRDWOOD.[1]

The diagnosis of megaloblastic anæmia depends on examination of the bone-marrow and the demonstration of megaloblastic changes in the erythroblasts and corresponding alterations in the granular leucocytes; no-one would now assume that an anæmia is megaloblastic because the red cells are macrocytic or hyperchromic, nor is the diagnosis excluded if the cells do not show these changes. The new methods are (1) biopsy of gastric mucosa by means of the instrument developed by WOOD, DOIG, and their collaborators [2] (this shows the state of the gastric mucosa, but since atrophic changes also occur in iron-deficiency anæmia,[3] the results are not conclusive); (2) estimation of the serum-vitamin-B_{12} level (biological methods are still the only ones available, using either *Euglena gracilis* [4] or *Lactobacillus leichmanii* [5] as the test organism); (3) a test of the urinary output of folic acid after a standard dose (this test has been developed by GIRDWOOD [6] and uses a biological technique with *Streptococcus fæcalis* as the test organism); and (4) the use of vitamin B_{12} labelled by a radioactive cobalt isotope to follow the absorption of a test dose of the vitamin.[7] Unfortunately none of these methods is suitable for routine laboratory use. The methods of microbiological assay are tricky and call for experienced staff, and the use of radioactive materials must be kept to a minimum. But by using these methods much has been learnt that can be applied clinically.

The nutritional megaloblastic anæmias are found principally in tropical countries, such as India, Kenya, Uganda, and Nigeria, or subtropical zones like Macedonia. Published records show that, judged by response to treatment, folic-acid deficiency is important in some places and vitamin-B_{12} deficiency in others; in fact, GIRDWOOD remarks that the cause differs not only from country to country but also in different areas in the same country. Modern methods have not yet been applied to the study of these anæmias on any large scale, and unfortunately difficulties in their interpretation have arisen. GIRDWOOD has found that a low urinary output of folic acid may follow a test dose when the primary deficiency is of vitamin B_{12}, and conversely output may be normal after an injected dose of folic acid when the patient's tissues are actually depleted of folic acid. Estimation of folic acid or vitamin B_{12} in the food is difficult because there are substances that have the biological activity of folic acid and vitamin B_{12} but not their hæmopoietic action; and it is also necessary to imitate closely the cooking processes normally used to prepare the patient's food. In tropical countries it is also very important to assess the effect of other conditions that may cause anæmia, such as hookworm infestation, malaria, and protein deficiency. For all these reasons, though we can make a fair guess at the likely classification and treatment of nutritional megaloblastic anæmia, we have as yet insufficient reliable information. On the other hand, in sprue and other "malabsorption" syndromes we have more to go on. In suspected sprue or steatorrhœa the fat balance can be estimated; but this is not too easy depending, as it does, on the proper consumption by the patient of the weighed diet and the efficient collection of stools over a period of from three to twelve days. GIRDWOOD's folic-acid test estimates the urinary output of folic acid after subcutaneous and oral doses of 5 mg. of synthetic pteroylglutamic acid. In idiopathic steatorrhœa there is often a considerable fall in urinary output after the oral dose, as compared with the fall after the subcutaneous dose, whereas in other conditions the difference is not very great; but the test does sometimes show poor absorption in patients who had normal fat balances. On the other hand, patients whose tissues are *not* saturated and who need folic acid can respond normally. On p. 700 of this issue, Dr. GIRDWOOD also records that it has not been possible to show any impairment of absorption of other members of the vitamin-B complex—riboflavine, aneurine, and pyridoxine.

The serum-vitamin-B_{12} level in patients whose tissues are not saturated with folic acid is normal—that is, above 130 $\mu\mu$g. per ml.—contrasting sharply with the patients with pernicious anæmia, whose serum-vitamin-B_{12} level is well below this figure. Measurements of the absorption of radioactive vitamin B_{12} have shown that in steatorrhœa the absorption is sometimes normal, but in about half the patients there is some defect, though not as severe as that in per-

1. Girdwood, R. H. *Quart. J. Med.* 1956, **25**, 87.
2. Wood, I. J., Doig, R. K., Motteram, R., Hughes, A. *Lancet*, 1949, i, 18.
3. Davidson, W. M. B., Markson, J. C. *Ibid*, 1955, ii, 639.
4. Mollin, D. L., Ross, G. I. M. *J. clin. Path.* 1952, **5**, 433.
5. Girdwood, R. H. *Brit. med. J.* 1954, ii, 954.
6. Girdwood, R. H. *Lancet*, 1953, ii, 53.
7. Heinle, R. W., Welch, A. D., Scharf, V., Meacham, G. C., Prusoff, W. H. *Trans. Ass. Amer. Phycns*, 1952, **65**, 214.

nicious anæmia. CALLENDER and EVANS,[8] reporting these findings, showed that some increase of vitamin B_{12} absorption in such patients can be achieved by giving gastric intrinsic factor. GIRDWOOD draws attention to an interesting group of patients with megaloblastic anæmia, free hydrochloric acid in the gastric juice, and normal fat absorption, who show defective absorption of folic acid and a normal level of vitamin B_{12} in the serum. These patients respond to treatment with folic acid and have undoubtedly been classified in the past as "refractory megaloblastic anæmia," because the liver extracts prepared for the treatment of pernicious anæmia contain only small amounts of folic acid. It has also been possible to find patients with defective folic-acid absorption who had not yet developed megaloblastic anæmia, and yet others who showed defective absorption of both the antimegaloblastic substances, folic acid and vitamin B_{12}. For this reason the clinician must watch patients with non-addisonian megaloblastic anæmia to see whether, in the long run, they need treatment with a combination of vitamin B_{12} and folic acid.

Investigation of megaloblastic anæmia associated with structural abnormalities of the gastro-intestinal tract gives results varying with the site involved. A total gastrectomy that removes all or most of the part of the stomach that secretes intrinsic factor produces a condition like that of true pernicious anæmia. CALLENDER et al.[9] showed that the absorption of radioactive vitamin B_{12} was reduced to the same extent as in classical pernicious anæmia. In GIRDWOOD's patients the serum-vitamin-B_{12} was very low in patients with megaloblastic anæmia, whether the patients had had total gastrectomy or some other operation, but folic-acid absorption tests usually gave a normal result. This is at variance with clinical observations that megaloblastic anæmia secondary to alimentary-tract lesions other than total gastrectomy usually responds to folic acid. This discrepancy is even more obvious in the megaloblastic anæmia of pregnancy, as seen in temperate countries like Great Britain, when it is not usually due to malnutrition. Clinical experience has shown that these patients do not respond to treatment with vitamin B_{12}, but do improve smartly after treatment with folic acid. GIRDWOOD estimated the serum-vitamin-B_{12} levels in 15 of these patients and found, as expected, that they were normal in every case. But the test for folic-acid absorption carried out on 18 patients was also normal, and GIRDWOOD is forced to the conclusion that "malabsorption of folic acid, in the form of synthetic pteroylglutamic acid, is not a feature of the megaloblastic anæmia of pregnancy." We have as yet no really satisfactory explanation for this anæmia. GIRDWOOD also describes a patient who had megaloblastic anæmia after treatment with primidone ('Mysoline'). This patient failed to respond to vitamin B_{12} but responded satisfactorily to folic acid; in this anæmia too the serum-vitamin-B_{12} level and the result of the folic-acid absorption test were normal.

From his extensive experience GIRDWOOD proposes a classification of megaloblastic anæmias that is really a list of all the possible combinations that may cause such an anæmia. The ordinary clinician does not need anything so elaborate, but the important new point that he can learn from these investigations is that there exists a "malabsorption syndrome," affecting vitamin B_{12} and folic acid, singly or together, that has a protean clinical picture. There may be no diarrhœa or other disturbance of bowel action, the fat balance may be normal; the patient simply presents with a megaloblastic anæmia and often free hydrochloric acid in the gastric juice. Such cases are not very rare and the patients tend to be younger than those with pernicious anæmia. If suitable tests can be arranged, the actual absorption defect can be identified: a low serum-vitamin-B_{12} or failure to absorb a proper proportion of labelled vitamin B_{12} indicates vitamin-B_{12} deficiency; and, if GIRDWOOD's folic-acid excretion test is abnormal, folic acid is to blame; but a normal result with this test does *not* exclude folic-acid deficiency. If these tests cannot be performed, treatment with vitamin B_{12} and folic acid given in sequence can give the clue. A dose of vitamin B_{12} of 300 μg. intramuscularly daily for three or four days should produce a clear reticulocyte response in five to seven days and a definite rise of hæmoglobin in fourteen days; if this fails folic acid is given, 90 mg. intravenously or intramuscularly, or 20 mg. daily by mouth, and a response should follow after much the same intervals. It is essential to give the vitamin B_{12} first. This diagnostic treatment can be carried out only *if the patient has received no previous treatment with vitamin B_{12}, folic acid, or liver preparations.* This underlines once again the vital importance of avoiding the use of all "blunderbuss" preparations and "complete hæmatinics" for the treatment of anæmias which have not been fully investigated. It is regrettable that, in spite of constant opposition both here and in America, some pharmaceutical firms continue to market hæmatinic mixtures containing folic acid or liver preparations, whose use they must know makes extra work for doctors and denies patients the best treatment, which can be founded only on a proper diagnosis.

8. Callender, S. T., Evans, J. R. *Clin. Sci.* 1955, **14**, 387.
9. Callender, S. T., Turnbull, A., Wakisaka, G. *Ibid*, 1954, **13**, 224.

Nuclear Explosions

ENOUGH (and more) has been made known in the past ten years about nuclear explosions to leave no doubt of the magnitude of the disaster should the nations embark on nuclear warfare; and there are reasons to fear that the continued explosion of test weapons, even at the present rate of firing, may bring grave dangers.[1] We welcome therefore every effort to tell people just what the risks are; and one of the latest documents that does so is that prepared by the Defence Science Organisation of the government of India.[2] The aim of this book is to "describe in broad terms the physical and biological effects of nuclear explosions;" and its publication may stimulate further sombre reflections on how many more bombs can be set off before irretrievable harm is done. The book is based almost entirely on data derived from "open" literature; and although it is not free from technical terms it gives a clear view of the kinds of nuclear reaction which can be used for weapons, and the type and scale of the effects that each may produce. The Hiroshima and

1. See *Lancet*, 1956, I, 999.
2. Nuclear Explosions and Their Effects. Publications Division, Government of India, 1956. Obtainable from India House, Aldwych, London, W.C.2, price 7*s.* 6*d.*

Nagasaki atomic bombs were rated as "nominal" and were both equivalent to about 20 kilotons of T.N.T. They were exploded about 2000 feet from the ground and the death-rate was about 90% within $^1/_2$ mile of ground zero (i.e., directly beneath the bomb), about 50% between $^1/_2$ and $1^1/_2$ miles, and 1% or less beyond $1^1/_2$ miles. At least 75% of the Japanese casualties were caused by physical injuries other than those resulting from ionising radiations. After an air burst of a nominal bomb, the hazards from local fall-out of radioactive material are relatively small; but from a ground burst the fall-out danger would be serious, and an area of about 100 square miles would be heavily contaminated; the shape of the area would probably be elliptical, depending on the speed and direction of winds up to a height of about 6000 feet.

In contrast to the nominal atomic bomb, which destroys primarily by blast, nominal high-yield thermonuclear bombs are predominantly radiation weapons. This does not mean that their high-explosive effect is not enormous: a nominal high-yield bomb is considered to be one of 20 megatons of T.N.T.—i.e., a thousand times the power of a nominal atomic bomb. The energy released is comparable to that of a big earthquake or hurricane. It has been estimated that a 20-megaton bomb would virtually destroy the cities of New York or London, and cause some $7^1/_2$ million casualties by blast alone. On top of this the local radiation damage, almost entirely due to external radiation, would be even more lethal. An area of 10,000 to 100,000 square miles, depending on the weather and other conditions, would be seriously polluted by fall-out in a matter of a few hours or a few days. To judge better what this means, 100,000 square miles can be compared with the total land surface of the Earth: it is only a little less than 1/500th part. In test explosions in unpopulated areas local fall-out is more or less eliminated by careful study of the weather; and under these circumstances only the unavoidable global fall-out may be harmful.[3] This global, and in some cases annular, or semi-global, fall-out, is inevitable after any nuclear explosion, whether "test" or "real"; and nearly all the delayed radiation hazards are a result of this fall-out. Radioactive strontium is the most alarming constituent of fall-out,[1] and the Indian book discusses its dangers in much the same terms as the recent report of the Medical Research Council committee.[4] Moreover, it says nothing to allay our concern [5] that harm may also be done by the radioactive iodine in fall-out.[6]

As for the genetic effects of nuclear explosions, the book points out the difficulties and uncertainties of making any confident quantitative assessment of what these are likely to be; but it also makes several important points. For the genes of man (and of all other living organisms that have been investigated) there is a "spontaneous" mutation-rate due to natural causes in the environment—mainly ionising radiations, heat, and certain chemical agents. Man is thought to have reached a state of genetic equilibrium in that new mutants appear at a rate which is balanced by their elimination from the race, since nearly all mutations are harmful ones. As early as 1927 MULLER [7] demonstrated that ionising radiations could cause mutations and this is now generally accepted; and so is the fact that mutations are in general harmful. It follows that any increased exposure to ionising radiations, as from fall-out, will artificially increase the mutation-rate. The size of the increase will depend on the amount of radiation received, and if this dose is small the increase may not be immediately detectable. There are a number of reasons why it is hard to detect an increased mutation-rate, and their relative importance cannot be assessed accurately in our present state of knowledge. These reasons were discussed in the report of the committee on genetic effects of radiation, prepared for the U.S. National Academy of Science,[8] and in the M.R.C. report. For one thing, the baseline mutation-rate in man can seldom be estimated with reasonable accuracy. Dominant genes responsible for such conditions as achondroplasia, and those responsible for sex-linked traits manifest only in the male, such as hæmophilia, can be directly measured. But only much less accurate indirect assessments can be made of the mutation-rate in recessive genes; and the great majority of viable mutations result in these recessive traits. Since extra radiation will simply cause more mutations and not anything novel, that is another reason why these mutations will not at first be detectable, particularly if they are world-wide in distribution. Although the extra mutations may be difficult to define and measure, the increased load of human suffering which they bring will be none the less real. Moreover, since many mutations are recessives, only a small part of the damage done by each mutation will appear in the first generation. These considerations and our present ignorance of human genetics in general make it impossible to say just how serious will be the consequences of continuing test explosions at the present rate. There is, however, at least one clear-cut conclusion, shared by the Indian organisation, the M.R.C. committee, and the U.S. National Academy of Sciences committee: the explosion of nuclear weapons must entail more mutations and that is a bad thing, leading to cumulative damage from generation to generation. No-one has authoritatively suggested that there is a safe additional level above the background dose, and opinion is divided about the increment that can be reasonably tolerated by the human race.

The Indian report is particularly valuable because it is more readily understood by the reader who knows little of physics or genetics than are most other comparable sources. We believe that the hazards of nuclear radiation, both from weapons and other sources, are still only vaguely appreciated by many people, so that this simple and balanced description of the facts, as they are at present known, is very useful. At the same time, it is clear that biological understanding of radiation effects is lagging behind nuclear development and that we must do all we can to redress the balance with speed and so remove at least some of our doubts—if not our fears.

3. Eisenbud, M., Harley J. H. *Science*, 1956, **124**, 251.
4. The Hazards to Man of Nuclear and Allied Radiations. H.M. Stationery Office, 1956. Cmd. 9780.
5. See *Lancet*, 1956, ii, 81.
6. van Middlesworth, L. *Science*, 1956, **123**, 982.
7. Muller, H. J. *Proc. nat. Acad. Sci., Wash.* 1928, **14**, 714.
8. *Science*, 1956, **123**, 1157.

Annotations

PROGRESS IN CEYLON

THE health of the people of Ceylon has undergone a remarkable improvement in the past decade. As Cullumbine [1] put it, "in one year the general death-rate fell from a level typical of Asian or backward countries to one comparable to that of the more prosperous and advanced countries." A survey [2] recently published by the Ceylon ministry of health further illustrates these advances and gives an interesting summary of the development and present state of the island's medical services, supported by well-presented statistical data. The general death-rate dropped from 20·2 per 1000 in 1946 to 10·9 in 1953 and has since dropped lower than that of the United Kingdom and France. The infant-mortality rate was reduced from 141 per 1000 live births in 1946 to 71 in 1953—that is, it was halved in eight years—while in the same period maternal mortality fell to less than a third of the previous figure.

Several things have been responsible for these outstanding achievements. One is the increasing expenditure on health services by the government of Ceylon since it achieved Dominion status in 1948. In spite of a rapidly increasing population, the amount spent per head was 11 rupees in 1953 compared with only 3 rupees in 1945. Another help has been the bigger staff of the health services and especially the improved training and equipment afforded by schemes developed by the Ceylon ministry of health, aided by the World Health Organisation and the Colombo Plan. But the effective control of malaria has made the most important contribution.

For many years malaria was the most prevalent disease, according to the yearly reports of the director of health services. In 1946, $2^3/_4$ million cases of malaria were reported—a morbidity-rate of 412 per 1000 population, with a death-rate of 1·8 per 1000 population. After 1947 the treatment of all infected persons was combined with dicophane (D.D.T.) spraying of almost every human habitation in the island, organised through 28 truck units, 17 jeep units, and 15 walking units. In eight years these measures reduced the morbidity-rate to less than 5 per 1000. Tuberculosis, one of the severe endemic diseases of Ceylon, has been tackled with equal industry. Between 1949 and 1955 16 B.C.G. teams Mantoux-tested over 2 million people—about a quarter of Ceylon's population—and nearly a million were given B.C.G. vaccination. Mass miniature radiography, which began in 1950, showed that 1% of the people examined had active tuberculosis; but the death-rate from tuberculosis was halved between 1951 and 1954. Ankylostomiasis, which damages the health of so many in Ceylon, sapping their energy, vitality, and resistance to disease, now has a greater death-rate than tuberculosis and is unfortunately more resistive to treatment. Until recently about a third of the rural population were undernourished because of their poverty. In 1954 16% of all the school-children examined showed signs of malnutrition. Defective nutrition affects not only the human but the bovine population of Ceylon so that each cow yields in a year an average of only 60 gallons of milk, compared with an average of over 600 gallons in England. The average daily consumption of milk per head in Ceylon is only 2 ounces. Dried milk is issued free daily to 250,000 people.

The improved health of the people of Ceylon is itself causing difficulties. The rate of natural increase of the population (the excess of births over deaths per 1000 of the population) was 28·5 in 1953, compared with 4·5 in the United Kingdom. This rate of increase is one of the highest in the world. It is therefore hard for the government of Ceylon to raise the general level of nutrition, education, or housing because each year more food, more schools, and more houses are needed just to keep pace with the rapid rise in population. The task is being tackled in part by redeveloping large areas in the north-eastern "dry" zone, which for centuries were made uninhabitable by malaria. Jungle areas are being cleared and ancient irrigation schemes, which a thousand years ago enabled Ceylon to support a population twice its present one, are being restored. Agricultural workers are being helped to settle in these colonisation areas. On the positive side, too, is the fact that healthy manual workers can produce more in a working day than those weakened by chronic ill health and malnutrition. Moreover, better education (about 75% of all children now attend school) will raise the technical efficiency of semi-skilled and skilled workers and lead to greater productivity. With its wealth of natural resources—mainly tea, rubber, and coconut—and a government planning the effective economic development of the country, Ceylon's prospects seem bright.

1. Cullumbine, H. *Lancet*, 1953, i, 1144.
2. Health Progress in Ceylon: a Survey. By D. M. DE SILVA, O.B.E., M.R.C.S., D.P.H., assistant secretary, ministry of health of Ceylon. 1956. Government Publications Bureau, Colombo. Pp. 60. Rs. 3.35.

NOTIFICATION OF INFECTIVE HEPATITIS

IN this country infective hepatitis is not a notifiable disease. In the United States "infectious hepatitis including serum hepatitis" was added to the list of nationally reportable diseases in 1952, and the data collected from then until the end of 1954 have been studied by Sherman and Eichenwald.[1] Deaths due to infective hepatitis have been separately recorded in America since 1949 and, in contrast to the "reportable" cases, deaths known to be due to serum hepatitis are not included. Many cases of hepatitis are not reported, particularly the non-icteric illnesses, and many deaths attributed to infective hepatitis are in fact due to serum hepatitis. Nevertheless, Sherman and Eichenwald have been able to show clearly a seasonal variation and a changing geographical distribution for which a progressive improvement in reporting cannot account.

Hepatitis was most prevalent in the late winter and early spring, and least so in summer. Deaths showed no seasonal variation, because so many of them were in reality due to serum hepatitis and because many fatal cases of infective hepatitis run a lingering course. The number of cases reported each year increased in the period 1952–54; this observation accords with an incidence rising and falling in waves covering several years, as has been noted in this country [2] and in Denmark.[3] Those under 15 years of age seemed most susceptible—a finding which confirms the conclusion based on the recent study of an epidemic in Georgia.[4] The sexes were equally affected; and mortality increased with age. In the childbearing years more women died of infective hepatitis than men, whereas after the age of 50 male deaths predominated. Sherman and Eichenwald did not calculate case-fatality rates because so many of the reported deaths were probably due to serum hepatitis. For the year 1954 there were over 30 cases of infective hepatitis in the United States per 100,000 of the population; in Scandinavia in that year the prevalence was about twice as great.[5] It seems probable that the figure for this country was of the same order.

1. Sherman, I. L., Eichenwald, H. F. *Ann. intern. Med.* 1956, **44**, 1049.
2. MacCallum, F. O., McFarlan, A. M., Miles, J. A. R., Pollock, M. R., Wilson, C. *Spec. rep. Ser. Med. res. Coun., Lond.* 1951, no. 273.
3. National Health Service of Denmark, Medical Report for the Kingdom of Denmark, 1952.
4. Barondess, J. A., Drake, M. E., Bashe, W. J., Stokes, J. jun., King, H. U., McCroan, J. J., Murphy, W. J. *Arch. intern. Med.* 1955, **95**, 633.
5. *Wld Hlth Org. Epidem. vital Statist. Rep.* 1954, **7**, nos. 3 and 12.

Infective hepatitis is economically an important disease which may prevent its victim from working for as long as two months, and then not all patients are free from residual disability. And it is a disease of which much of the adult population has had antigenic experience, as is shown by the prophylactic efficacy of gamma-globulin given to contacts.[4 6] The agent of infective hepatitis is passed in the stools and is probably spread by ingestion of material contaminated by fæces [7]—a mode of infection which has been shown to work in volunteers,[8] and which is no doubt at least partly responsible for the rapid dissemination of the disease in poor hygienic conditions.[9] Some of these characteristics are reminiscent of poliomyelitis; but the prevalence of poliomyelitis in this country was only 4 per 100,000 of the population in 1954 and 18 per 100,000 in the peak years of 1947 and 1950.[10] Yet poliomyelitis, a more spectacular disease, is not only notifiable but the figures are recorded in a special table in the Registrar-General's weekly returns.

If infective hepatitis has hitherto had less attention than it deserves, it is probably because its study is so unrewarding. With no susceptible laboratory animal and no susceptible culture tissue, the search for sources of virus and for individuals carrying antibody has been very limited. It is to be hoped that the work of Rightsel et al.,[11] which we recently discussed,[12] will provide means for detecting hepatitis virus in the laboratory, so that it will be possible to identify chronic active infections without jaundice whose victims are acting as carriers,[13] and to select non-immune contacts for prophylaxis with gamma-globulin. Notification would help us to make the best use of such new weapons.

A SOUTHERN ARABIAN SYNDROME

In many undeveloped parts of the world it is hard to make thorough medical examinations because the population are antagonistic or indifferent; and a scientific inquiry into a particular disease is further hampered by difficulties over post-mortem examinations. Under such circumstances, incomplete observations which do not add up to any clear-cut picture of disease are none the less acceptable, and may point the way to rather empirical but still useful therapeutic advances. A recent example is the description by Fawdry [14] of a mixed syndrome in Southern Arabia among a chronically undernourished population riddled with malaria and schistosomiasis. In these people, severe anæmia, wasting, and enormous spleens rapidly develop. Medical treatment does little good, but removal of the spleen has been dramatically successful. Splenectomy is well suited to the mentality of the patients, but it taxes the restricted surgical powers of Southern Arabia. Although it was rarely possible to follow the patients for long, in 2 cases the immediate improvement was maintained for at least six months.

During the operation, biopsies of the liver were taken, and these showed that this condition is not simply a late stage of portal cirrhosis. Some patients were cirrhotic, but in the 2 successful cases there was no gross cirrhosis, though an increase in the hepatic reticulin was noted. Liver biopsy in 50 cases showed great variation from normal to gross fibrosis; severe fibrosis was regarded as a contra-indication to splenectomy. The anæmia was usually normocytic; the iron content of millet, the staple grain of the district, is so high that Fawdry rarely sees iron-deficiency anæmia apart from hæmorrhage.

The syndrome has some points of similarity to the picture of fibrosis of the liver in West African children [15]; and rather similar obscure splenomegalic anæmias have also been described in African populations whose diet is poor and who are infested by parasites of several kinds. Ordinary methods of treatment are nearly always ineffective without extensive public-health measures; but Fawdry has shown that surgery has a place in the treatment of these unfortunate people.

JUST CAUSE

When an operation is performed by a competent surgeon, whatever the risk, there is usually just cause for running that risk; so the consent of the patient is full justification for what would be otherwise an aggravated assault. But the law has always frowned on wounding, even with consent, where the subject is rendered less useful to the State as a result. The law regarding this matter has lately been ably reviewed by Minty.[16]

No-one can say whether the law of mayhem still exists. Mayhem is the ancient crime of so injuring a man that he becomes of less service to his king and country. Consent was no defence to mayhem, as is shown by an old case of a young man who persuaded his friend to cut off his hand so as to avoid work. This was plainly a mayhem. The modern principle seems to be that consent is no defence if the injury inflicted is injurious to the public as well as to the person injured. Public injury, however, need not necessarily be physical hurt, as in mayhem. Prohibition of prize-fighting was intended, not to prevent damage to a useful citizen, but to avert the riotous behaviour which so often accompanied prize-fights. Duelling, in which the object is to kill or seriously injure the other party, is clearly illegal despite consent by both sides. In the case of sport where there is an element of risk, but in which personal injury is not the objective, there is the advantage to the community of healthy exercise of physical skills. Applying these principles to surgery it is obvious that almost all surgical operations, by saving life and health, are a benefit to the community as well as to the individual. Plastic operations on severely disfigured patients may not save life, but they restore confidence and often return the victim to useful work. The position of cosmetic operations for removing sagging skin is more debatable. It is arguable that there may be some benefit to the person by improving her mental outlook, although a new hat might do just as much good. The more reasonable view is that there is no just cause for such operations of vanity, but they are still unlikely to injure the public. Though the surgeon runs a slight risk of civil action if his efforts fail to please, he would probably not expose himself to prosecution for unlawful wounding. A principle seems to emerge that there must be just cause for any surgical operation on healthy, if ageing, tissues.

But operations on the sexual organs must be considered apart. Induction of abortion is a crime, but the just cause of saving maternal life or health permits this in proper circumstances. Sterilisation in the female is likewise legitimate with proper indications, the more so because contraceptives are not entirely reliable. It is in the matter of male sterilisation that the question of public injury arises. Vasectomy is perfectly lawful as a means of preventing the transmission of hereditary disease; and as part of the operation of prostatectomy it is necessary to prevent orchitis. In a recent case (Bravery *v.* Bravery) the Judge discussed the question

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of the legality of male sterilisation solely to free sexual intercourse from consequences. By depriving the State of possible future citizens this is clearly injury to the public. A surgeon proposing to sterilise a man, with consent, purely to prevent conception, may risk prosecution for unlawful wounding.

RADIATION DAMAGE TO THE LUNGS

THOUGH radiotherapy has long been used for mammary cancer and intrathoracic neoplasms, serious trouble from radiation of the lungs seems rare. For example, Hutchison,[1] in a search of the archives of a large general hospital, found only 1 unequivocal case in a quarter of a century. On the other hand, slight X-ray damage to the lungs, producing only transient changes in chest films, is probably quite common.[2 3] The patient who has symptoms may have an acute febrile illness with cough, frothy sputum, dyspnœa, and cyanosis, sometimes strikingly accentuated by exercise. Recovery is usual, but when the inflammatory reaction in the lungs has been severe and extensive, death may result rapidly or after a more or less prolonged period of respiratory insufficiency. The onset may also be insidious with dyspnœa and cyanosis on exertion as the main features. Accompanying changes in the radiological picture of the lungs may be a localised or diffuse haziness, often fanning out from the hilum, or the appearances of infiltrating disease.[1–9]

Clearly many patients with radiation damage are unsuitable subjects for detailed investigation; but Stone et al.[10] report that in 2 out of 5 cases in which the diagnosis was confirmed by subsequent pathological examination they were able to carry out complete lung-function studies. The essential findings were diminution of vital and total lung capacities and impairment of oxygen diffusion through the alveolar membrane—findings in keeping with those previously reported in radiation damage[9 11 12] and in lung fibrosis associated with other conditions.[12–14] The results of arterial blood-gas analysis in 2 further cases—low values for oxygen and normal values for the much more readily diffusible carbon dioxide—also pointed to interference with gaseous exchange across the alveolar membrane. These abnormalities are readily accounted for by the results of examination of the lungs in these and other cases.[1–3 6–8 15–17] It seems that first there is damage to the alveolar walls and capillary endothelium with, in the more acute conditions, an outpouring of exudate which may form a hyaline membrane closely applied to the alveolar wall.[18] Later the alveolar walls are thickened by fibroblastic proliferation, and peribronchial and perivascular fibrosis also develops. This picture is not specific for radiation damage, and may be distorted by coexisting malignant disease or infection, so that a conclusive diagnosis of radiation fibrosis is seldom possible.

In the treatment of the condition, the administration of oxygen and antibacterial drugs are obvious measures; and as there had been favourable reports of corticotrophin and cortisone therapy[9 19] Stone et al.[10] tried it too in all their cases. They considered that it prolonged the life of 2 patients with acute disease, but it failed permanently to arrest the downward progress in any case. They suggest that the prophylactic value of cortisone be assessed; but this would be difficult, for although advanced age, arteriosclerosis, and pulmonary infection have been thought to predispose to radiation damage,[3 20] in fact, individual susceptibility seems to vary greatly and unpredictably. Moreover, although symptoms usually arise within a few weeks of stopping radiotherapy, the onset is sometimes considerably delayed.[1 10] Stone et al. believe that the greater the volume of lung radiated, the larger the amount of radiation delivered, and especially the shorter the period over which the dose is given, the more likely is it that trouble will ensue; and careful consideration of these points is probably the best preventive measure. The rarity of serious radiation damage in the past is reassuring, but Stone et al. point out that because of the increased power of modern equipment vigilance is now more than ever necessary, and as Whitfield et al.[18] observed, it is important that clinicians should be aware that damage may follow radiotherapy in which the customary dose is not exceeded.

HYALURONIDASE AND SCARS

THE Central Scientific Investigation Institute of Traumatology and Orthopædics at Moscow is under the direction of Prof. N. M. Priorov, the doyen of Russian orthopædic surgeons, who has just celebrated his 70th birthday. A recent paper[21] from the institute records some results of enzyme therapy in dealing with the sequelæ of trauma. Experiments on rabbits and mice have shown that hyaluronidase solution applied to the skin so increases its permeability that penicillin applied at the same time is absorbed into the blood-stream. The hyaluronidase is not toxic, it has not produced anaphylaxis, and it has shown little antigenic power. On the other hand, when injected subcutaneously, hyaluronidase has considerable antigenic properties and stimulates the formation of neutralising antibodies. Priorov et al. conclude that, for clinical use, external dressings soaked in a solution of hyaluronidase powder dissolved in a physiological solution should be applied. This method was tested on 117 patients with different types of scars (postoperative, post-traumatic, burns, and keloid), Dupuytren's contracture, tenosynovitis, joint contractures, and unhealed ulcers. 56% of the results were good, 23% were satisfactory, and the remainder of the conditions were unchanged. The results were best where the scarring was of short duration, and less good when the scarring had been present a long time or in well-established Dupuytren's contracture. Priorov et al. also suggest that the method might be used for skin necrosis caused by ionising radiation.

THE MANAGER OF THE LANCET

Mr. F. G. H. Holt has retired from the post of Manager and Secretary of THE LANCET. Joining our staff, from Oxford Medical Publications, in 1921, he has worked for the journal during more than a quarter of its existence; and none has served it more loyally. Through eventful and often difficult years, he has never spared his efforts or lowered his standards; and as Manager since 1929 he has handed on the LANCET tradition to his juniors.

Mr. W. E. Hurren succeeded Mr. Holt as Manager and Secretary on Oct. 1.

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Special Articles

DESIGN OF CRASH HELMETS

J. S. P. RAWLINS
M.B.E., M.A., B.M. Oxfd
SURGEON LIEUT.-COMMANDER, R.N.
From the Royal Air Force Institute of Aviation Medicine, Farnborough, Hants

ACCIDENTS involving racing motorists and motor-cyclists have focused public attention on the need for head protection, and opinions expressed regarding existing types of crash helmet have often been based on empirical views and established misconceptions rather than on scientific experience.

I review here the very considerable research concerning the frequency, site, and mechanism of head injury, and examine the fundamental requirements of crash-helmet design in the light of the experience gained in the development of the Mk. I Protective Helmet now in general use in the Flying Services.

Before considering the design of crash helmets it is first necessary to know the incidence of head injury; the sites of injury and the relative frequency with which they are involved; and the effects of injury at these sites.

Incidence of Head Injuries

Crash helmets are worn mostly by aircrew, motor-cyclists, and racing motorists. The frequency of head injuries in the Royal Air Force was assessed in 1943; 40% of all crash injuries were craniofacial, and 20% of all fatalities were due to head injury.

In 1953 a review of accidents in the United States Air Force showed that 24% of all major injuries were head injuries and 14% of fatalities were due to head injury. For motor-cyclists Starks (1952) showed that more than 50% of major injuries involved the head. In these latter series figures were obtained for injuries with and without head protection, and the results are given in table I, which shows that the wearing of a crash helmet reduces both the proportion of fatalities due to head injury and the proportion of major head injuries by roughly 40%.

Sites of Head Injury

In the 1943 series of 485 head injuries there were 200 cases of concussion and 85 scalp wounds. Such relatively minor injuries can be expected to be completely prevented by a suitable helmet. Of the graver injuries 93 were fractures of the base, of which 85 were fatal. Of the remainder over 50% were fractures in the frontal region.

Cairns and Holbourn (1943) listed the sites of impact in 96 cases of head injury among motor-cyclists and related them to the effects on skull and brain. Then he concluded that (1) the frontal region was most commonly injured; (2) the vertex was least commonly injured; (3) occipital blows were least dangerous; and (4) temporal blows were most dangerous. This relates only to motor-cycle injuries where the occiput is probably only damaged on rebounding from the object struck. Fatal occipital injuries have occurred in accidents in flying and motor-racing when the back of the head has been brought into violent contact with the seat squab.

TABLE I—RELATION OF HEAD INJURY TO HEAD PROTECTION

—	No. of persons with major injury	Persons with primary major head injury (%)
U.S. Air Force 1953:		
Helmets not provided	618	24·3
Helmets provided..	289	14·2
	No. of persons with fatal injury	Fatalities due to head injury (%)
Helmets not provided	215	14
Helmets provided..	915	7·4
	No. of persons with major injury	Persons with primary major head injury (%)
Motor-cyclists 1952:		
Helmets not provided	198	51·5
Helmets provided..	163	27

It has not been possible to obtain figures for head injury among racing motorists, but they are probably similar to those among aircrew. At all events it is possible to conclude that (1) in all these activities head protection is an obvious requirement; (2) the helmet should be designed to give maximal protection to the frontal area; (3) protection must be adequate in the temporal region; (4) occipital protection is necessary for aircrew and racing motorists; and (5) protection of the vertex in motor-cyclists is of secondary importance.

Mechanics of Brain Injury

Denny-Brown and Russell (1941) experimentally produced concussion in animals by allowing pendulums of different effective masses to strike the head. With the lighter pendulum no concussive effect could be obtained when the head was fixed. When it was permitted to move as little as 3 mm. however, there was concussion.

Holbourn (1943), who investigated the physical mechanism of brain injury, using artificial brain sections of gelatin framed in a paraffin-wax "skull," found that the maximal strain was produced in the temporal region as a result of rotational accelerations applied to the "skull." This was because the rotating "skull" exerted its maximal turning force on the "brain" at the point where the temporal lobe was gripped by the lesser wing of the sphenoid. He concluded that the main causes of head injury were: "(1) deformation of the skull with or without skull fracture; and (2) sudden rotation of the head which is responsible for the so-called contrecoup injuries, for some extracranial hæmorrhages, and probably for concussion." He also pointed out that the finding by Denny-Brown and Russell (1941) that concussion was difficult to produce unless the head was allowed to move confirmed his view that rotational acceleration was the significant factor.

Gurdjian and Webster (1945), who studied experimental concussion in morphinised dogs, found that "in direct violence (i.e., with the head fixed), injury is due almost entirely to deformation of the skull with consequent generalised compression of intracranial structures," and "intracranial dysfunction is caused by first, a sudden setting of the head in motion, and second, deformation of the skull." Regarding contrecoup lesions, they examined 72 head injuries at human necropsies and stated "a majority occurred on the orbital surfaces of the frontal lobes, the temporal tip and the lateral aspect of the temporal lobe on one or both sides. The preponderance of contusions in this neighbourhood is caused by the many bony irregularities of the orbital surface of the anterior fossa, and the knife-like edge of the lesser wing of the sphenoid." The distribution of the lesions, although attributed by these workers to the classical contrecoup mechanism, provide striking confirmation of Holbourn's (1943) theory.

Pudenz and Shelden (1946), who substituted 'Lucite' domes for the calvaria of monkeys and recorded the effect on the brain of blows to the skull, found that (1) with the head free to move, the cortex glides within the calvarium, rotating mainly in the sagittal and horizontal planes; (2) with the head fixed there is little or no gliding of the cortex (linear acceleration);

(3) for all blows the parietal and occipital parts of the brain move farther than the frontal and temporal parts; and (4) brain movement is much greater following blows in the parietal and temporal regions than following blows in the frontal and occipital regions. The first three findings appear to be in accordance with Holbourn's (1943) theory and suggest that linear acceleration is of lesser significance. The last finding is in accordance with the observation of Cairns and Holbourn (1943) that blows in the temporal region are the most lethal.

In summary it appears that brain injury results from (1) direct penetration of the skull; (2) deformation of the skull with or without fracture; (3) rotational acceleration; and (4) linear acceleration (probably to a smaller extent).

A crash helmet designed to protect against brain injury should therefore be tough to prevent penetration and relatively rigid. To minimise the danger of rotational acceleration the surface should be free from all projections and should have as low a coefficient of friction as possible. It will naturally tend to prevent such acceleration from being transferred to the brain by itself rotating about the head.

Mechanics of Fracture of Skull

The brain can be injured without fracture of the skull, and the skull can be fractured without injury to the brain. To design a crash helmet to protect against fracture of the skull it is necessary to know the impact energies and approximate accelerations at which fracture will take place.

Much research has been done on this subject, ranging from the dropping of cadaver heads to the catapulting of plastic head-forms against various structures. The results have established that the skull is fractured when one of the following conditions is present:

(1) A 5 ft. fall on to concrete (cadaver-heads).

(2) An average deceleration of 200–300 g.

(3) A peak deceleration of 500–700 g. (equivalent to a peak force of 5000–7000 lb. for a 10-lb. head).

(4) Kinetic energy of impact of 500–700 inch-lb.

(5) Rate of rise of acceleration of roughly 200,000 g. per sec. (Chandler 1953).

An additional factor is impact force per unit area. It is apparent that, for a given force, the smaller the area of application the greater are the chances of fracture or penetration.

Therefore, to protect against fracture of the skull, a helmet should absorb the kinetic energy of the moving head by converting it into energy of either extension or compression. It should reduce the average linear deceleration by extending the duration of the impact, and the peak linear deceleration by ensuring a linear rate of rise of g. Preferably it should limit the rate of change of acceleration and it should distribute the force of an impact as widely as possible over the head.

Accelerations in Accidents

If an aircraft travelling at 150 ft. per sec. crashed into a solid object and the nose structure collapsed evenly, with the result that there was 10 ft. of uniform failure of metal, the pilot would be subjected to 30 g. Now, if the pilot's head is unsupported, it may be assumed that, as the aircraft decelerates violently, the velocity of his head will surpass that of the aircraft by perhaps 64 ft. per sec. If it strikes a rigid object it will be decelerated over a distance of the thickness of the scalp, say $^1/_4$ in. before the skull achieves uniform velocity with the object struck. Thus the deceleration of the skull will be roughly 3000 g. If the object struck—e.g., the instrument panel—deforms for 1 in., the acceleration is quartered—750 g. If a crash helmet can be provided which will allow uniform deceleration over $^1/_2$ in., this figure is reduced to 500 g. and may now be survivable.

Roth (1952) records experimental head-on crashes between two cars driven by members of a stunt team. The cars were driven from the rear seat, the drivers throwing themselves behind the front seat just before the impact. With relative velocities of 60·4 m.p.h. the decelerations of the cars varied between 12·2 and 16·1 g. Compared with the acceleration of the ejection seat (17 g.) and Stapp's high-speed trolley (50 g.) these decelerations are quite small and are due to the extensive crushing (about 3 ft. per car) which took place. If the driver's head were in contact with a solid portion of the car at the time of the impact and throughout the period of deceleration, no damage would be sustained.

In motor-cycle accidents the driver usually leaves the machine with an initial velocity equal to that of his machine and is finally stopped by collision with another object or by friction due to sliding along the ground. With a wide range of initial velocities the deceleration of the driver's head will vary from 2 or 3 g. in the case of a slide to tremendous decelerations when a man travelling fast collides head first with an approaching vehicle.

Thus a motor-cyclist thrown from his machine at 100 m.p.h. and striking a wall head-first would have an average acceleration of more than 16,000 g. applied to his skull. It is obvious that no crash helmet can ever make the full range of motor-cycle accidents survivable.

British Standards

When the efficacy of a crash helmet is called into question as the result of an accident in which it failed to afford protection, great emphasis is laid on the fact of its having passed or failed to pass the specification of the British Standards Institution. Usually, if it has passed, the manufacturer is exonerated from all blame, and the injury is accepted as inevitable.

Currently there are three standards applying to crash helmets which are basically the same except that the test provisions for racing helmets are more stringent than those for helmets for everyday use. It is beyond my present scope to criticise the test provisions of these standards in detail, but several points are noteworthy.

In the first place the distinction drawn between the two types of helmet is unrealistic. The unprotected skull fractures with a peak force of 5000–7000 lb., corresponding to an impact velocity of 12–13 m.p.h. The best commercially available helmet can reduce the peak force at this velocity to less than 3000 lb., which is equivalent to raising the critical impact velocity for fracture of the skull by only about 4 m.p.h. That such an increase is of practical value is shown by the comparative figures for head injuries with and without protection, but it is surely illogical to suggest that the ordinary motor-cyclist travelling at speeds up to perhaps 50 m.p.h. is less likely to meet with an impact of this order than his racing counterpart travelling more than twice as fast; and it is quite certain that, with any helmet, a direct impact at anything over 50 m.p.h. will be unsurvivable.

Other points are that the impact test used is equivalent to a peak force of roughly 3000 lb., which is only about half that necessary for fracture of the skull; and there is no test for either energy absorption or resistance to abrasion. Hence helmets which have passed the specification of the British Standards Institute may vary enormously in their ability to absorb an impact and may be softened or destroyed by a brief exposure to abrasions. The latter fault has been clearly illustrated in racing accidents. A new standard is in course of preparation, but it is desirable that wearers of helmets to the present standard should be aware of the limitations of their equipment.

Design of Crash Helmets

The requirements of the ideal crash helmet may now be summarised and related as far as possible to practical design as follows :

(1) Protection against penetration and abrasion.
(2) Protection against deformation of the skull.
(3) Reduction of rotational acceleration.
(4) Reduction of average linear deceleration.
(5) Reduction of peak linear deceleration.
(6) Absorption of kinetic energy.
(7) Distribution of impact.

In addition, of course, the crash helmet must be as light as possible, comfortable, cool to wear, and efficiently secured to the head. Further modifications will be imposed by the special requirements of the activity for which it is designed.

To meet the requirements listed above, the helmet should have the following respective qualities :

(1) It should be tough.
(2) It should be rigid, not elastic.
(3) Its surface should be free from projections to minimise torque.
(4) Its surface should be smooth and have a low coefficient of fraction to facilitate sliding over the opposed surface.
(5) By uniform deformation it should smooth out the acceleration curve.
(6) It should convert kinetic energy to energy of compression or extension.
(7) It should spread the blow as widely as possible over the head.

Some of these properties are mutually incompatible. In practice, therefore, the helmet can never be ideal. However, by regarding the helmet as being composed of two parts, an outer shell and an inner lining, something approaching the theoretical ideal can be imagined.

The Shell

For the outer shell many materials have been examined, from stainless steel to natural cork. Steel is excellent against penetration but is incompressible and therefore transmits virtually all the kinetic energy of a blow. Cork provides excellent absorption of impact but gives no protection against penetration. Between these two extremes lie various plastics, wood-pulps, and shellac-impregnated fabrics, but the most suitable material yet tested at the Royal Aircraft Establishment is undoubtedly resin-bonded continuous-filament nylon, which is used in the Service Mk. I helmet, which is light, very tough, and relatively rigid, and will withstand successive heavy impacts each of which causes delamination, and in doing so expends part of its energy. Under test at Farnborough one shell has so far withstood without obvious deterioration 55 impacts from a 10 lb. weight dropped from 10 ft. on to the crown. Such a shell will protect against penetration and deformation of the skull and reduce rotational and average linear accelerations.

The Lining

The shell may be lined with a harness, with padding, or with a combination of the two. It is convenient to consider them seperately.

Harnesses are generally used. They are easy to manufacture, they are cool, and their adjustability simplifies sizing. Their greatest value lies in distribution of impact ; and, with a properly designed harness, a local blow on the outer shell can be distributed all over the head. If a harness is used, great attention must be paid to the stitching and to the attachment to the shell. Preferably the harness should not fail under a survivable impact ; ideally it should stretch but yet prevent the shell from making contact with the head.

In aircrew helmets comfort and coolness are of paramount importance, and for that reason a harness was used in the Mk. I helmet. Nylon tape of 1000 lb. breaking-strain was used, and the harness was held by duralumin plates riveted to the inside of the shell. Nylon tape will extend permanently under a shock-loading and is therefore particularly suitable for this purpose.

The objection often made to the presence of metal plates inside the shell (that they may be driven into the scalp) has not been substantiated in practice. In fifty accidents in which the helmet has played a part, ranging from mild to extreme impacts, this has never happened.

Padding.—Such is the range of padding materials now available that it is probably true that a material can be found which will weigh less than a good harness. Padding provides the best absorption of impact and is fairly easy to manufacture, although separate moulds or formers may be required.

For the Mk. I helmet samples were tested by sandwiching them between two brass plates and delivering a measured blow from a pendulum. Accelerometers in the striker and on the plates recorded the peak accelerations delivered and transmitted across the sample.

The best material tested was a sandwich of expanded polyvinyl chloride of soft and medium density ; it was three times as efficient as sponge rubber.

Road Research have made further tests on padding materials at various temperatures and with repeated blows. They confirm the value of expanded polyvinyl chloride, but show its deterioration at high temperatures. Better materials are cellular polystyrene and natural cork.

Table II is adapted from their figures and shows the peak force transmitted by samples $^1/_2$-in. thick when subjected to a blow from a 10-lb. wood block travelling at 15 m.p.h. It also shows whether the behaviour of the samples is affected adversely by temperature, and the approximate cost per c. ft. The best material tested, from the point of view of absorption of impact, lightness, and stability in a range of temperatures was foamed polystyrene ; the materials beneath the dotted line in table II are clearly unsuitable. More than thirty specimens were tested in this way, and as a result a manufacturer can, by referring to Road Research's figures, immediately select a material of suitable performance, density, and cost for his purpose. There appear to be no arguments for persisting in the use of sponge or expanded rubbers.

TABLE II—PEAK FORCE TRANSMITTED BY $^1/_2$-IN. SAMPLES SUBJECTED TO A BLOW FROM A 10 LB. WOODEN BLOCK TRAVELLING AT 15 M.P.H.

Material	Peak force (lb.)	Density (lb.c. ft.)	Cost per (c. ft.)	Affected by temperature
Medium soft expanded p.v.c.	5000	54·5	3*s.*	Yes
Foamed polystyrene	6000	3·5	..	No
Natural cork	6000	27·3	4*s.* 5*d.*	No
Compressed cork	7500	33·3	2*s.* 6*d.*	Slightly
Expanded rubber, open-cell—dense	15,000	63·9	7*s.* 6*d.*	No
Expanded rubber, open-cell—medium dense	15,000	64·8	9*s.* 6*d.*	No
Expanded rubber, closed-cell—soft	15,000	67·4	4*s.*	No
Extra soft expanded p.v.c.	15,000	68·4	2*s.* 4*d.*	Yes
Expanded rubber, closed-cell—dense	17,500	77·4	3*s.* 6*d.*	No

Conclusions

Research on materials has provided the necessary knowledge for the construction of crash helmets narrowly approaching the theoretical ideal, and the principal limit to the efficiency of commercial helmets need only be that imposed by economic considerations. At present the best material tested for the shell is continuous-filament resin-bonded nylon. The best material for the

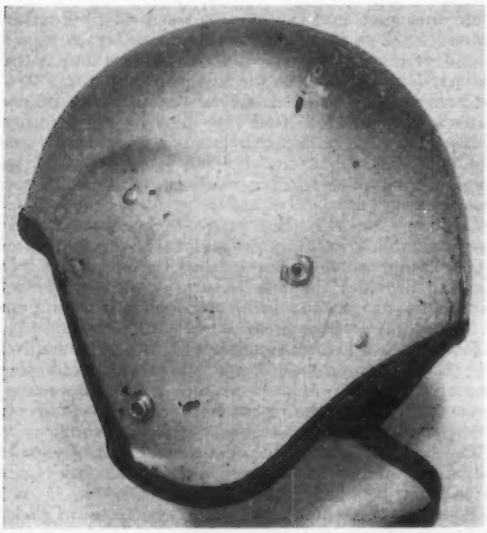

Fig. 1—Helmet worn by civilian pilot in major accident involving repeated impacts. Damage to helmet includes 3-in. crack in cervico-occipital region and stellate cracks radiating from left frontotemporal angle.

Fig. 2—Helmet of naval pilot whose aircraft inverted on take-off and struck the ground upside-down. Note section broken outwards in left frontotemporal angle.

lining is probably expanded polystyrene, and the rigidity of the shell will spread a local impact over a wide area of the lining and hence of the head. Further distribution of impact could be obtained by using a light-weight harness or net whose sole object is to keep the head clear of the padding (incidentally permitting air-circulation thereby) but having a degree of stretch which will allow the head to bottom on to the shock-absorbing lining in the event of a heavy impact. Such a helmet is at present under development.

The technique of moulding nylon is admittedly expensive and unsuitable for mass-production by relatively unskilled labour, but laminated fibreglass is very efficient and can be moulded in the cold; 'Durestos' has a poorer strength-weight ratio but is still efficient and can be cast in concrete moulds.

As regards the padding, expanded polyvinyl chloride of various densities is roughly a third the cost of sponge rubber; natural cork roughly a half.

It is impossible to resist the conclusion that efficient crash helmets could be put on the market at commercially satisfactory prices.

Illustrative Cases

Whatever methods are used to test helmets in the final analysis, only their behaviour in actual accidents can supply a true measure of their value. In the past there have been many reports showing how head-injury statistics have been altered by the wearing of crash helmets, but relatively few accounts give details of individual accidents in which a crash helmet played or failed to play a part. Each of the following cases illustrates a point in the foregoing remarks on helmet design.

Case 1.—A motor-cyclist not wearing a crash helmet collided with a car, and a protruding door-hinge penetrated his skull, entering the frontal lobe. The impact was not great, for damage to both vehicles was minimal. Had the cyclist been wearing a helmet with a hard smooth outer shell, his head would have slid off the hinge and impacted the door panel. A cork helmet, on the other hand, would almost certainly have availed him nothing.

Case 2.—A civilian pilot force-landed on an air-field at 190 knots. The aircraft bounced nineteen times before slithering through a caravan site and breaking into three pieces. The pilot's Mk. I helmet (fig. 1) had a 3-in. crack in the cervico-occipital region and a circular indentation $^1/_8$-in. deep in the right temporal region in addition to other cracks. Apart from severe shock the only injury to the pilot was a small cut on the right eyebrow. This illustrates the resistance of nylon to penetration and to repeated impacts, properties which are rare in most commercially available helmets.

Case 3.—Just as an aircraft became airborne, the starboard wing folded, with the result that the aircraft rolled over on to its back and hit the ground. The impact smashed the 'Perspex' canopy and fired the ejection seat. The automatic release gear was subsequently carried away, allowing the pilot to be thrown clear. The pilot's helmet (fig. 2) was

Fig. 3—Helmet of naval pilot whose aircraft crashed into funnel of aircraft carrier and fell upside-down on flight-deck. Helmet shows evidence of very severe blow in right parietal region with rupture of nylon fibres.

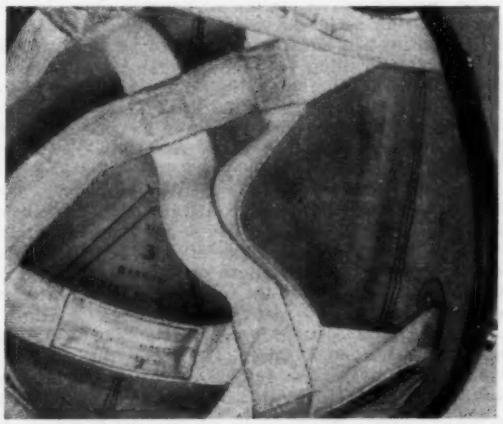

Fig. 4—Imprint of harness on inner lining of helmet, showing that shell had deflected on to head. Pilot recovered.

abraded, and a piece was broken outwards from the left frontal angle. The pilot lost consciousness momentarily but was passed fit for flying-duties in four days. Nylon is extremely tough and is not softened by abrasion even at speeds in excess of 100 m.p.h.

Case 4.—An aircraft stalled during an attempted carrier-landing and crashed into the ship's funnel. The nose remained imbedded in the funnel, the rest of the fuselage breaking off and falling upside down on the steel deck some 30 ft. below. The cockpit canopy was shattered on impact with the deck, and fire broke out, which was rapidly brought under control. The pilot was extricated unconscious. The Mk. I helmet showed evidence of a very severe blow in the right parietal region with rupture of some of the nylon fibres, and lesser damage on the left side (fig. 3). The stitches of the anterior fixation point of the harness had ruptured, and there was a clear imprint of the harness on the leather lining of the shell, although the harness could not be made to bottom on to the shell (fig. 4).

The pilot sustained a fracture of the right parietal, not depressed, with separation of the coronal suture. There were bilateral hæmatomata of the scalp over both parietal bones, fracture of the body of the fifth cervical vertebra with evidence of C5 and C6 lesion, and a comminuted fracture of the right tibia and fibula. The pilot was unconscious for eleven days but has since made a complete recovery and has returned to duty.

This accident represents the borderline between success and failure of protection for the helmet. Had the impact been a little more severe, it is doubtful whether the pilot would have survived. The implication is that the construction of the helmet is sufficiently strong to withstand a maximal survivable impact, yet the shell deflected inwards on to the harness. Though this must represent considerable absorption of energy, it is questionable whether by using polystyrene padding with or without the harness the parietal and vertebral fractures might have been prevented.

Case 5.—On overshooting, a Hunter aircraft struck a hangar and broke in two. The forward portion with the cockpit rolled over the hangar and crashed upside down on the ground. The canopy was shattered, and the unconscious pilot was found still strapped in his seat. He died ten hours later. His Mk. I helmet showed evidence of a very severe blow on the vertex (fig. 5), and the harness was torn away in the frontal region (fig. 6).

The overriding factor in this case was that the pilot was wearing a helmet which was much too big for him. It would therefore have been hanging from the chin-strap at the moment of impact, and would have decelerated before the pilot's head took up the slack in the harness. It therefore received a much greater shock-loading than that for which it was designed, and consequently the stitching failed.

The implication is that crash helmets must be fitted carefully if a harness is used, the correct fit being the tightest fit compatible with comfort.

Summary

Most present-day crash helmets are based not upon scientific theory but upon established lines which have resulted from misinterpretation of the mechanism of head injury.

When the physics of head injury are studied, it is immediately clear that a theoretically sound helmet is neither difficult to design nor necessarily expensive to manufacture.

Although the shape and details of a properly designed crash helmet may vary with the purpose for which it is intended, its basic properties will always be the same—resistance to penetration, resistance to deformation, reduction of accelerations, and absorption of kinetic energy.

I am grateful to the Medical Director-General of the Navy and to the Director-General of Medical Service of the Royal

Fig. 5—Helmet of pilot whose aircraft struck a hangar and crashed upside-down on hard-standing. Evidence of severe blow with rupture of fibres in right parietal region.

Fig. 6—Nylon harness torn from anterior attachment, allowing helmet to bottom on to head. Pilot was killed.

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THE HEALTH SERVICE IN 1955

INTRODUCING his Ministry's report[1] for 1955, Mr. Robert Turton, the Minister of Health, points to three main tasks now facing the National Health Service: "first, to bring existing hospitals to a satisfactory standard and to provide, as far as possible, new accommodation as and where it is needed; second, to ensure that the mental health services, with their proportion of out-of-date buildings, receive a proper share of the new construction and the resources available; finally, to tackle the problem of making adequate provision for the care of old people." The main administrative problem was undoubtedly that of coöperation between the different branches of the service. The solution lay, as the Guillebaud committee had recognised, in finding the best way of encouraging more teamwork rather than in making changes in organisation. This was particularly true in the field of the domiciliary services and preventive health. Mr. Turton summarises the conclusions of the Guillebaud committee by saying that though there are weaknesses the structure of the service is sound, the question of any fundamental change is premature, and

TABLE I—HOSPITAL WAITING-LISTS BY SPECIALTIES, DEC. 31, 1954 AND 1955

Specialty	Waiting-list (thousands)		Percentage reduction
	1954	1955	
General medicine	8·8	8·1	11
General surgery	127·8	121·4	5
E.N.T.	146·7	134·3	8
Gynæcology	58·3	57·5	1
Tuberculosis	3·0	1·39	54
Chronic sick	9·7	9·3	4
Traumatic and orthopædic surgery	34·6	35·4	2 (increase)
Plastic surgery	13·4	13·5	0
Thoracic surgery	4·6	3·3	28
Neurosurgery	3·0	2·8	7
All non-mental specialties	465·0	442·0	5
All specialties	474·0	453·0	4·5

the need for stability over a period of years, without prejudice to minor adjustments, is important. He hopes that all associated with the service will have noted with satisfaction but "without complacency" the committee's view that "the Service's record of performance since the Appointed Day has been one of real achievement."

HOSPITAL SERVICES

The Ministry's report records that by the end of 1955 hospital waiting-lists were 25,000 lower than in any year since the beginning of the National Health Service. During the year the total waiting-list dropped from 474,000 to 453,000. The reduction was not of course uniform (table I). By far the largest reduction was among those waiting for tuberculosis treatment—a 54% drop compared with the previous year. In most areas there is no longer a real tuberculosis waiting-list.

1. Report of the Ministry of Health for the Year Ended Dec. 31, 1955. Part I. 1. The National Health Service. 2. Welfare, Food and Drugs, Civil Defence. Cmd. 9857. H.M. Stationery Office. Pp. 254. 9s.

The number of inpatients and outpatients is still increasing and, as in the previous years, the reduction in the waiting-lists must be attributed to an improved use of beds and other resources available. At the end of the year the number of staffed beds available for patients was almost exactly the same as at the end of 1954 and the only explanation of the increased number of patients treated is that more patients were treated per bed during the year (table II). In mental hospitals although the number of beds increased by over 1000 during the year the number of patients discharged increased by a greater proportion so that the same principle applied. The better use of beds was due to a reduction in the average length of stay of each patient rather than a reduction in the turnover intervals between patients (table III).

The total number of new patients attending outpatient departments dropped from 11,366,000 in 1954 to 10,595,000 in 1955. The number attending consultative clinics went up by nearly 75,000 and the reduction in

TABLE II—NUMBER OF PATIENTS DISCHARGED OR DIED PER ALLOCATED BED, 1954 AND 1955

Group of patients	Non-teaching hospitals		Provincial teaching hospitals		London teaching hospitals		All hospitals	
	1954	1955	1954	1955	1954	1955	1954	1955
Other than mental and mental deficiency	12·3	12·5	22·0	21·7	17·7	17·6	13·1	13·2
"Acute" (i.e., other than mental, mental deficiency, chronic, and chest)	17·7	17·4	22·9	22·6	18·5	18·4	18·1	18·1
All patients	6·8	6·9	21·9	21·6	17·1	17·0	7·5	7·6

the total is accounted for by a 20% drop in the number attending casualty departments, "the reason for which is not yet clear."

HOSPITAL STAFF

The number of consultants employed in 1955 increased by 140 to 6650 and the number of senior registrars employed was 1094 compared with 1120 a year before. The number of distinction awards in England and Wales recommended by the standing advisory committee and current at Dec. 31, 1955, was 266 A awards (£2500 per annum), 665 B awards (£1500), and 1330 C awards (£500).

MENTAL HEALTH SERVICES

"The problems of the mental health services are among the most difficult of those facing the Minister." At the end of 1955 there were 139,440 patients in designated mental hospitals, excluding former Public Assistance institutions. On recognised space standards these hospitals should accommodate only 121,475 patients. The average overcrowding was 14·8%. The degree of over-

TABLE III—AVERAGE DURATION OF STAY IN HOSPITAL (DAYS), 1954 AND 1955

Specialty	1954	1955
General medicine	22·8	22·2
General surgery	13·7	13·6
E.N.T. (*a*) other than tonsils and adenoids	8·1	8·1
(*b*) tonsils and adenoids	4·2	4·4
Gynæcology	11·1	11·2
Diseases of the chest	151·7	142·1
Chronic sick	177·8	171·6
Traumatic and orthopædic surgery	26·7	26·1
Plastic surgery	18·1	17·6
Thoracic surgery	32·0	31·0
Neurosurgery	20·2	18·6
Mental illness -		
(*a*) treated under the Lunacy and Mental Treatment Acts	608·0	552·2
(*b*) others	107·1	78·0

crowding varies between hospitals from nil to 64·9% but "the overall shortage gives a fair indication of the gravity of the position." At the end of 1955 the number of beds in use in mental-deficiency hospitals was 47,387—an increase of 566 during the year. There were 51,334 patients in residence so that the accommodation in use was overcrowded by 8·3%. At the end of the year the names of 6909 mental defectives were on the waiting-lists for hospitals, compared with 7033 at the end of 1954. "The number of mental defectives who are waiting for hospital care and training is still considerable and more than half are urgent cases, but the schemes that have been planned for providing additional beds during the next few years will go a long way towards meeting the needs."

Up to the end of March, 1956, regional hospital board programmes have provided for 8700 new beds (3300 mental and 5400 mental deficiency). Apart from further beds being provided out of the ordinary capital allocations 6800 (2400 mental and 4400 mental deficiency) are included in the programme of major schemes, already started or projected, which is being financed centrally.

The report draws further attention to the fact that improved treatment facilities both clinical and social are needed. Many mental hospitals are about a hundred years old and few are "designed and equipped fully to meet modern medical requirements or to provide the better living and social conditions which are now accepted as essential." Much has been done to remedy the defects, but much still remains to be done and special allocations for capital expenditure have been made for modernisation of mental and mental deficiency hospitals. These amount to £500,000 for 1956/57 and £1 million for 1957/58 in addition to the normal allocations.

HEARING-AIDS

During the year the number of people fitted with hearing-aids for the first time was 53,617, bringing the total since the beginning of the National Health Service to 466,195. The waiting period remains little more than nominal. The report refers to successful clinical field trials of a model capable of being used with miniature batteries in the amplifier case or, like existing models, with separate batteries. It was later found, however, that it would be possible to accelerate the introduction of transistors into the hearing-aid service and it was therefore decided early in 1956 to drop the valve monopack programme and wait for the even smaller and more convenient and economical transistor aid.

BLOOD-TRANSFUSION

The number of people on the panel of blood-donors (591,204) showed an encouraging net increase of 50,815, but the demand for blood continues to grow and still more regular donors are needed. The number of donations of blood also increased from 700,202 in 1954 to 759,571 in 1955.

CHRONIC SICK

The results of a survey undertaken in 1954 of the services for the chronic sick and elderly showed that more than half of the hospital management committees in England and Wales had some beds specifically allocated to their treatment. The total number has been increasing since the beginning of the N.H.S. and by the end of 1955 had reached 54,000—about 1·2 beds per 1000 population. The distribution is, however, uneven. Nearly two-thirds of the beds were occupied by women. It is doubtful whether, taking the country as a whole, there is any real shortage of beds. Although the waiting-list for chronic sick beds at the end of 1955 was 9273, "there is not the least doubt that many chronic sick waiting-lists are grossly inflated."

It is estimated that nearly 4500 people occupying chronic sick beds no longer required hospital care but could not be discharged because other suitable care and accommodation was not available for them. Moreover, about 2000 old people in "welfare" accommodation provided by local authorities ought to have been in hospital. "There is unquestionably room for improvement," the report says, in the arrangements for exchanges between hospitals and old people's homes.

GENERAL PRACTICE

During 1955 the number of admissions to executive councils' medical lists was 990, giving a net increase of 256. Of those admitted 606 entered into partnerships. The total number of doctors practising as principals in England and Wales and providing unrestricted general medical services on July 1 increased from 18,528 in 1954 to 18,832 in 1955. On July 1, 1955, there were 6715 practitioners practising single-handed and providing unrestricted medical services. In 1954 there were 6899 and in 1953, 7147. These figures suggest that the gradual movement away from single-handed practice has continued although it is now slackening. On the same date there were 12,068 doctors practising in partnership—an increase of 485 on a year previously. The south of England was still the most popular part of the country for doctors. The average number of applicants for vacancies in the north was 36, in the midlands 38, in the south 58, and in Wales 20. Applications to start new practices in "designated" areas in the north fell from 36 in 1954 to 30 in 1955 and applications to practice in partnership from 119 to 87.

The distribution of doctors in relation to the numbers of patients is "improving satisfactorily." In "designated" areas 3671 doctors were practising compared with 4224 in 1954, but the number of patients living in such areas dropped from about 11½ million to a little over 10 million.

PRESCRIBING

During 1955 statistics were supplied to many executive councils for the doctors in their areas showing the average cost of a doctor's prescribing compared with the average for the area in which he practised. These local statistics were welcomed in most areas. As a result of these statistics more doctors were visited by regional medical officers and more letters written to doctors about the cost of their prescribing than in 1954. During the year visits were made to 543 doctors and letters sent to 1225, compared with 345 visits and 353 letters in 1954. 1955 was, however, the first year since the reintroduction of formal investigation of excessive prescribing in 1950 that no cases were formally referred to the local medical committees for investigation.

During the year 226,116,091 prescriptions were dispensed by chemists—7,403,276 more than the 1954 total. The total cost of the prescriptions was £49,120,365 at an average cost per prescription of 52·14*d.* (in 1954 the average cost was 50·44*d.*). The number of prescriptions was the highest for any year since the service began, with the exception of 1951 when there was an epidemic of influenza; but in 1955 there were no serious epidemics. The average cost per prescription is likely to have been affected by the fact that doctors were able to prescribe some comparatively expensive new preparations—e.g., chlortetracycline (aureomycin) and oxytetracycline (terramycin).

COST OF THE SERVICE

The total cost of the National Health Service for England and Wales was about £495 million in the

financial year ended March 31, 1955. Nearly four-fifths of this was met by the Exchequer out of moneys voted by Parliament. The total cost of the service was about £22 million more than in the previous year. There were increases in the cost of most services, particularly the hospital and specialist services, due both to rising prices and increased use. No new charges were imposed during the year, and payments by persons using the service were approximately the same as in the previous year, though they represented a slightly lower proportion of the total cost.

In 1954–55 payments made by patients to dentists and opticians of the charges for dental treatment, dentures, and glasses amounted to slightly less than £6·9 million for dental treatment and dentures, and slightly less than £4·9 million for glasses; those for drugs and appliances amounted to slightly more than £6 million; and those paid to local health authorities (for example, for attendance at day-nurseries or for the provision of extra food, nursing, and sick-room equipment during illness and convalescence) were estimated at about £2·4 million.

ASSOCIATION OF INDUSTRIAL MEDICAL OFFICERS

THE association's 21st anniversary meeting was held in London on Sept. 24–28. At a reception at Canterbury Hall Sir WILSON JAMESON invested the president of the association, Dr. R. S. F. SCHILLING, with the new jewel, a portrait of Charles Turner Thackrah in enamel on gold and silver. Sir Wilson recalled that twenty-one years ago some half-dozen industrial medical officers sought his advice about the formation of an association. He counselled them to avoid medical politics and to develop their activities on the lines of a dining club. He believed this had remained the policy of the association and in large measure accounted for its unprecedented success. Opening the inaugural meeting, Mr. IAIN MACLEOD, Minister of Labour and National Service, referred particularly to the work of the industrial health advisory committee which sat regularly under his chairmanship. Two pilot investigations had been initiated, one of a general kind in Halifax and the other concerned with a specific industry in Stoke-on-Trent.

HEALTH PROBLEMS OF THE OLDER WORKER

Although dealing primarily with his experience in Swedish industry, Prof. SVEN FORSSMAN drew attention to the increasing proportion of old people in countries with high standards of living. The effect of ageing on physical strength was not so important now as formerly, because of mechanical devices for lifting, carrying, and loading, as well as rationalisation. The reduction in mental working capacity by ageing may be compensated by greater experience and better planning of work. There were two groups of elderly people—those in very good health and those who survived illnesses such as diabetes and tuberculosis thanks to better medical treatment. Professor Forsmann had carried out a study in eight industries with 20,000 employees. Most old employees, whether salaried or wage-earning, wished to continue their work after the usual age of retirement and this was unrelated to pension rights. Examinations by industrial health officers showed that 50–70% of all old employees had impaired health and reduced working capacity. The main reasons were diseases of the circulatory system (55%) and of the organs of movement (20%). Those who had transferred to light work had done so because of diseases of the respiratory, circulatory, and digestive systems. The average total absenteeism was about the same for old employees as for younger workers. Those engaged in light work had a higher rate of sickness absenteeism than those in heavy work, probably because of the tendency to employ the healthier workers on heavy work in the first instance. The productivity of the older worker, judged by working time, absenteeism, and earnings, compared favourably with that of the average worker. The elderly should not be "teamed" with the youthful, especially on piece work. They should be allowed more frequent rest pauses and longer lunch periods. There should be a flexible retiral age, but not so as to hinder promotion. Regular health examinations were important.

ASSESSING THE HEALTH OF THE INDUSTRIAL WORKER

In the MacKenzie industrial health lecture Dr. SCHILLING said that the industrial medical officer formerly confined his attention to disease, but now he was called upon to assess other physical factors. Epidemiological methods were used to measure hazards by looking at occupational groups, and the results could be applied to individuals. In order to find examples for teaching students Greenhow (1858) consulted the Registrar-General's published figures. He examined mortality and morbidity rates and personally conducted field surveys. For example, he compared the death-rates, for those over the age of 20 years, per 100,000 of the population in Haltwhistle (where there were no lead mines), and in Alston and Reeth (where there were lead mines):

	Males	*Females*
Haltwhistle	374 ..	583
Alston	1440 ..	779
Reeth	1298 ..	717

Recently, Morris and his colleagues were able to show that coronary disease was commonest among sedentary workers. Schilling's investigation into the cotton industry revealed an excess mortality from cardiovascular-renal disease among strippers and grinders. Sickness-absence statistics were not used with sufficient care. They could be misleading because, for one thing, recorded sickness did not depend entirely on pathology. Field surveys depended upon the coöperation of the population. One could not assume disease in people who had not been seen. Observer errors in clinical and radiological signs were also very important.

RESEARCH IN OCCUPATIONAL HEALTH

The EARL of VERULAM spoke on the scope for a new approach by management. There were five categories into which all jobs may be divided. (1) *Sedentary*. There was no responsible source of information, readily available, about the best way to sit at work. "Anatomical seats" were cheaper than latex-sponge seats, but they seemed to imply that all anatomies and all jobs required the same type of seat. The adjustable back-rest was used only as a rest and not as a support for work. (2) *Peripatetic*. The machine-builder makes a virtue of the fact that all the controls are on one panel. It was probably healthier to exercise all the limbs most of the time than to over-employ a few muscles all the time. "They shall walk not faint," said Isaiah. (3) *Peculiar*. Many people adopted unnatural working positions—for example, the coalminer, the cowman, and the clockmaker. Coal-cutters allowed the miner to move about more, cowmen stood at a lower level than the cows, and the relative positions of clockmaker and his supplies of components were changing. (4) *Asymmetrical*. The human body was biologically an organism that was bilaterally asymmetrical. Machine lay-outs compelled a man to work in a lop-sided manner. (5) *Mobile*. One aspect of safety on the roads was the colour of vehicles. Manufacturers of cars chose colours which were smart or fashionable; and lorries were coloured to suit advertising needs.

Sir HAROLD HIMSWORTH emphasised the need for "liaison investigators" in research. There were two

types of research, the one basic and aimed at increasing knowledge and the other practical and dealing with the particular. Both points of view were proper and necessary. But there was a need for men who talked both languages, men with interlocking skill. An important example was the obvious need for research in aviation medicine, but little progress was made until the Institute of Aviation Medicine was formed. This institute represented an example of research in occupational medicine: it was a prototype. Many problems could be investigated on the spot; others must be referred to laboratories. The machinery usually took the form of a committee. Broad policy required a forum, but there must be users plus liaison investigators plus basic scientific workers. No-one could control research except the man who was doing it, but research could be influenced by informed knowledge. The members of such a committee were not mutually exclusive. Small organisations could not sustain research. It might be possible to group related industries—e.g., various textiles—for this purpose.

Sir ALFRED ROBERTS said that the need for a comprehensive occupational health service underlay all discussions on occupational health, including research. There should be (1) a coördinated Government policy and (2) a substantial increase in the resources devoted to occupational health. As to the first requisite, the responsibility should rest with the factory department of the Ministry of Labour. Resources should be increased by more medical inspectors of factories and equipment, extended medical supervision by employing more doctors in industry, and the institution of an industrial hygiene service on the lines of the Federal Laboratory Service in the United States. Research fell broadly into two stages: (1) identification and on-the-spot investigation of occupational health risks; and (2) long-term laboratory research. Research-workers should take the unions into their confidence. The unions would probably provide money to establish *prima-facie* cases, but they would expect a vigorous follow-up from the Government. Ignorance of the part played by working conditions and rheumatism had been described as "a vital gap in contemporary knowledge." There must be constant and well-informed pressure from outside the Ministry from all those concerned with occupational health, from trade unions, management, research-workers, and doctors working in industry.

USE OF ATOMIC ENERGY

Dr. KATHARINE WILLIAMS referred to the Government's statement that the new industry of nuclear energy was a major industrial development which would bring with it revolutionary changes in technique. This would lead to intensive research in metallurgy, ceramics, and resins. Isotopes were being used as sources of radiation and as tracers in research. Industrial research laboratories were finding radioactive tracers invaluable in studies of problems such as friction, lubrication, diffusion, and a wide range of chemical processes. The penetrating power of radiation was the basis for the use of thickness gauges, whether for sheet metal, paper, cardboard, plastic, film, or tinplate coating on steel. Warning signals betrayed differences in levels and fillings of packets as they passed on a conveyor belt. Radiation sterilisation of some pharmaceuticals, food, tissues, and packaging materials, with little temperature change, would be possible within the next decade. The eradication of insects infesting grain and flour and the inhibition of sprouting in potatoes would be among the earliest applications. Irradiation of ova or one of the parents could cause infertility in the offspring. In the sphere of plastics, polymerisation could be induced with pressures little above atmospheric and at ordinary temperatures. γ-ray vulcanisation of rubber caused the molecules to link together without the intervention of sulphur and in the cold. In medicine, radioisotopes would not alter the present approach to the treatment of disease, but they would extend and refine methods already in use. It was the use of radioactive tracers in biological research which was having the most profound effects, in particular in tracing the pathways of biosynthesis. There was also likely to be a revision of concepts in plant nutrition and fertiliser practice.

OCCUPATIONAL MEDICINE IN A TEACHING HOSPITAL

In his John C. Bridge memorial lecture, Prof. R. E. LANE stressed throughout that industrial medicine was a part of general medicine, but he suggested that a department devoted to this subject could improve the services a hospital gave its patients, broaden medical teaching, and contribute to medical research. He opposed any attempt to segregate "industrial" cases, which should, for the most part, be seen in the general clinics of the hospital. But he maintained that in an industrialised area it was necessary to provide a consultation centre to which cases could be referred for advice. Such a department would make itself particularly familiar with the health problems of local industry. He described his own clinic at the Manchester Royal Infirmary. An analysis of the patients referred showed that 60% were sent for diagnosis and 40% for advice on resettlement at work. Chronic respiratory disease provided a large proportion of patients in both categories. Professor Lane was against adding further burdens to the medical student, but he thought that during routine clinical teaching the place of occupation in ætiology and in therapy should be borne constantly in mind. He illustrated the type of research problem likely to be encountered and stressed the need for epidemiological and environmental investigations on certain situations disclosed by clinic patients. In the absence of Government funds for such work, he advocated the formation of institutes of occupational health on a voluntary basis.

MENTAL HEALTH IN INDUSTRY

Dr. R. F. TREDGOLD discussed the uses of psychiatry in management training. Various methods were used in training courses; visual and auditory methods should be combined. The audience should participate by taking part in discussions. The main group should be split into syndicates small enough to allow the less vociferous an opportunity to speak. Rôle-playing gave more insight and stimulated freer speaking. Films were not used as much as they should be. A delicate technique, and one often used accidentally, was deliberately to give a bad lecture to stimulate emotions. It was better to raise resistance and deal with it.

Mr. A. HERON, M.SC., dealt with psychological research in industry. In cases of marginal mental health, such as mental deficiency and chronic psychosis, it was not true to say the patients were industrially unproductive. They seemed capable of payment by results even if we had lost touch with them and may despise them. In the United States there was unity on what was now called the "second industrial revolution." Electronic engineering would alter the function and structure of industry to a greater degree than many people alive today were willing to believe. The middle-aged must learn new jobs. Some mental ill health was inevitable. Research in this direction was a necessity, not a luxury.

Speaking on work, payment, and capacity, Dr. ELLIOTT JAQUES defined "time-span of discretion" as the maximum period an employee could carry on with his job without guidance. The significance lay in its connection with fair rates of pay. It was not based on known rules, but was evolved by members of a company

working out a theory intuitively. It suggested an unrecognised national wage structure and neglect of it led to disputes. A second factor was the failure to distinguish underpayment from under-usage—that is to say, work below the employee's capacity. Separation of these two factors had helped to clarify disputes. Underpayment was often settled by consideration of the level of work performed by the group. Under-usage called for consistence with growth in capacity. It was found that normal earning growth curves resembled biological curves. Individuals tended to predict their earnings in terms of these growth curves: in other words, the price an employee put on his services was the same whether he admitted to being ambitious or affected that he was resigned to simple rewards.

At the anniversary dinner, on Sept. 27, Sir Harry Platt, F.R.C.S., proposing The Association, recalled that its foundation had given rise to misgiving in other branches of the profession. Now it had established its place in the sun. What of the future? Would industrial medical officers remain few—a corps d'élite—or would they increase in number to help form the comprehensive occupational-health service which had been the great dream of the late Ernest Bevin? However development took place, he hoped that it would not be development in isolation. In his reply Dr. R. S. F. Schilling, the president, declared that the association was expanding greatly because the enlightened employer and the trade unions realised the importance of good medicine in industry. The industrial medical officer's function was to serve the whole of industry. The Earl of Verulam, proposing Medicine in Industry, said that the industrial medical officer's professional neutrality was increasingly recognised. Dame Florence Hancock responded for The Guests to a toast proposed by Dr. L. G. Norman.

Public Health

Poliomyelitis

UNCORRECTED notifications of poliomyelitis in England and Wales in the week ended Sept. 22 were as follows: paralytic 39 (46), non-paralytic 72 (66); total 111 (112). This is a decrease of 1 compared with the previous week, the figures for which are in parentheses. Notifications remain well below the average for the past nine years. The proportion of non-paralytic cases is high.

Improving Water-supplies

In a circular to statutory water undertakers in England and Wales, the Minister of Housing and Local Government asks them to consider combining with their neighbours in an effort to improve the efficiency of the water-supply system.[1] The Minister feels that the process of regrouping, which has been going on gradually since the Water Act, 1945, was passed, should now be tackled more quickly and radically. "Many undertakers, although they have met the needs of their consumers admirably in the past and are justly proud of their record, are likely to find their resources no longer equal to the tasks set by the growing demand for water from domestic, industrial, and agricultural consumers." The Minister is "looking for substantial progress in the next 12 months."

Tuberculosis in Eire

The latest annual report[2] of the department of health for Eire remarks on a "spectacular decline" in the tuberculosis death-rate—from 91 per 100,000 population in 1949 to 34 per 100,000 in 1954. New cases coming under the notice of health authorities decreased only from 7552 in 1949 to 6266 in 1954. The department urges that young tuberculin-negative people should be protected by B.C.G. vaccination, particularly if they intend to move from the country to large towns. In the five years up to the end of 1954, more than 1300 people returned from Britain to undergo treatment for tuberculosis in Eire.

1. *Times*, Sept. 28, 1956.
2. Report of the Department of health, 1954–55. Obtainable from the Government Publications Sale Office, G.P.O., Arcade, Dublin. Pp. 88. 3s. 6d.

In England Now

A Running Commentary by Peripatetic Correspondents

Coelum non animum mutant qui trans mare currunt. The old tag seems to be as true, or as false, when the sea-crossing is done by air. In other words, Madrid hasn't yet made any particular inroad on my preconceptions. (If it comes to that, even the "coelum" hasn't been changed all that much—to a Mancunian, even by adoption, it is a fine sight to see the rain lashing on the Puerto del Sol.) I think a good plan for the visitor to Madrid would be to bring his helicopter and stay in Toledo, where the streets are largely old and narrow and cobbled, and the cars are limited to a few streets only. This hypothetical visitor could then land daily on the top of the Prado at opening-time, and avoid the streets entirely. For those of humbler pocket, I would commend the Metro, where the course of traffic is both dignified and stereotyped. There really isn't much in Madrid besides the Prado, and if there is I haven't seen it. But the Prado certainly makes up for it. Apart from the trio of El Greco, Velasquez, and Goya, most schools are represented (I believe there is a Reynolds snugly tucked away in the attics). There are also three whole works by Hieronymus Bosch (masquerading as Bosco), which anyone who saw the Flemish exhibition at the Academy will want to see. There is no point in a catalogue, however—to me the lovely thing was the way in which when you went from the gallery to the buffet, the folk in Goya's paintings had already stepped from their frames, and were there with you, waiting to be served, or possibly even serving you.

* * *

His father died the day before his 100th birthday and his grandfather lived to 103. Is it any wonder that old Bingle, at 94, considered himself a mere chicken? After his bout of pneumonia we sent him to *Blackstones*—a large tumble-down house miles from nowhere, where sixty old men eke out their remaining span.

Old people need a corner of their own, and Bingle found his corner quickly. "I'm not stoppin' here unless I can work," he declared. Matron understood—besides, she was short of staff. A remarkable worker he turned out to be. He made his bed, he swept the floors, he cleaned the cutlery ("the silver" he called it), and tended his little patch in the garden. Then, at the end of the day's work, came his special privilege and his alone. With rolled-up sleeves and apron, he would sit in the kitchen with Cook, a glass of beer at his elbow and a smouldering pipe in his mouth. He never said anything but just sat impassive, like any honest labourer at home when day is done.

One morning he awoke with a streaming cold. Amid noisy bouts of coughing and sneezing, he prepared to follow his normal routine. He was donning his apron when Matron saw him. Pleading, argument, and persuasion all fell on deaf ears. All his life he had never stopped work for a common cold and he saw no reason to change his ways. Their voices rose, words became harsh. "But you are old!" cried Matron, like the young man in *Alice*, and snatched the apron, which he was clutching desperately, from his grasp. With a terrible rending sound, one half of it came away in her hands. At this Bingle grew quiet and allowed himself to be hustled back to bed.

When dinner was served, he was missing. A search of the house and grounds was begun at once but it was futile, for his bed was tidy and his locker bare. There was no help for it but to inform the police, and search parties were soon under way. He was found the same afternoon, stick in one hand and his few belongings in the other, having covered nearly ten of the thirty miles to his daughter's cottage. They brought him back unrepentant and defiant.

I was glad he got no further. Now he need never know his daughter has been gone these six months—she was over seventy when she died. He need never know his loneliness.

For us, as for many other families no doubt, this has been a memorable summer.

On a particularly cold June day Third Child fell in the river. She floated past me, face down, her best gaberdine billowing above her. Giving hardly a thought to my sensible tweed coat and thick shoes, I plunged in up to the waist and hauled her out with such speed that her first horrified gasp was air and not water. She was crosser and wetter than one would have believed possible. Me too.

On one of the few fine balmy summer evenings my husband got home to find an outsize flood in the road. He and our elderly black Rover (car, not dog) had to pick their way through mixed sewage and the children's bath water, owing to a sizable block in our main drain. The unblocking strained all our resources, and the subsequent decontamination set us back half a bottle of 'Dettol' and all my remaining eau-de-cologne.

On the eighth day of our fortnight by the sea First Child changed from rather spotty to unmistakably chickenpox, and so we started for home. On our way, on a particularly crowded part of A30, Third Child choked on a piece of apple I'd given her to quieten her (little guessing how nearly it would). She turned a deep purple and ceased to breathe. Calling in no uncertain terms for a halt and medical aid, I fished up to the elbow in her throat, finally dislodging the apple. She paled to violet and gave a crow or two, just as my husband managed to get the car off the road and sprang out, with that expression on his face which means I-was-trained-in-one-of-our-best-medical-schools-and-am-prepared-to-do-a-tracheotomy-with-the-picnic-knife-if-necessary. Fortunately need wasn't, as she became a mere li[illegible] and started to yell. After her feelings were soothed she slept peacefully till we got home, so perhaps a good choke is *the* method for quietening children in cars.

Fourteen isolated and quarrelsome days later Second Child produced a fine crop of spots, easily diagnosed, and thirteen even more isolated and quarrelsome days after that, Third Child succumbed to the virus.

Still, winter can't be far behind.

* * *

I want you to put me an' t' lad an' t' misses on yer panel. We're not satisfied wi' t'other chap.

What's wrong ?

It's the lad. Look at t' brid' of 'is nose !

M' nose is alright, Dad.

Shurrup or I'll lam thee on t' lug. *I'm* tellin' doctor what's wrong wi' thee. An' 'e's coughin' an' barkin' . .

No I aren't.

. . . an' 'eaving 'is 'eart out . . . sick in yer waitin' room.

That were nowt. M' gob-stopper got stuck

Now 'ave a care Sam ! 'ave a care ! I'll lam thee. An' 'e picks 'is nose an' me an' 'er 'ave told 'im but 'e won't lay off. 'Eadstrong ! Put that instrument down or doctor'll slice thee up. Always on a fidgit. An' you can see 'ow 'is nose is ever on t' drip. Wipe it, Sam !

Wot wiv ?

An' she wants to know if owt can be done about them eyes. They call 'im scissors at school . . . an' 'e's very sensitive : very sensitive is Sam.

Jack Rag started that, Dad. But I got 'im.

Eh ?

I poured m' school dinner down 'is Wellington.

That's another thing. Won't eat. She gave 'im jellied eels for breakfast an' pig's cheek for tea an' 'e puts 'is nose up at it. *I* think it's the gastric.

Tell 'im about yer ulcer, Dad.

I'm tellin' 'im about *thee* at t' moment. I'll tell 'im about m'sel' in a bit.

Tell 'im about Ma's catarrh, then.

Qui-ert ! 'Ow can doctor sort thee out w' thee chiggin' an' bleatin' all t' time ? An' stop scrattin'. 'E's wick wi' worms. Now will you put us on yer panel ?

Why do you want to leave your other doctor ?

Well I 'ad to call 'im out last night to t' missis . . . it's 'er catarrh ; an' 'e said 'e didn't think the call was necessary. She were right upset because that there catarrh 'as plagued 'er for years. So I said to 'er this morning I said, Right, old flower, we'll take our custom helsewhere !

* * *

Brain-washing is here. The architect has now given us an Endoctrinology Lab.

Letters to the Editor

SPREAD OF ANTIBIOTIC-RESISTANT BACTERIA

SIR,—As you say (Aug. 11), this problem is becoming increasingly important. Staphylococci are the prime offenders, but strains of *Escherichia coli* associated with infantile gastro-enteritis are also suspect, and, as you remark, hæmolytic streptococci of Lancefield's group A may be protected by fellow-travelling penicillinase-producing staphylococci. It is significant that these resistant strains are most commonly found in hospitals. Whereabouts in hospitals are they developed and stored ?

The answer is that the strains are developed in patients. The storage sites are varied. The tainted thermometer (Sept. 15, p. 559) is one. Another could be baths,[1] and yet another the umbilicus.[2] More capricious reservoirs of infection are the mattresses incorporated in the beds of patients. The concertina effect of alternate compression and relaxation, as the patient moves in bed, as the nurse makes adjustments and makes the bed, and if heavy objects are placed on the bed and removed, all cause infected air to be sucked into the interior and then ejected into the bedclothes. The pillow is just a smaller form of mattress, and is pummelled and punched, ejecting its quota of infected air, as the nurses make the bed or the restless patient moves. Blankets are the third important reservoir in the bed. Dust on the floor, on shelves, on locker-tops, on the architraves of doors and other ledges, carry their quota of resistant organisms. Nearly always forgotten are the cups, mugs, plates, cutlery, and the humble dishcloths with which these things are "cleaned," wiped, or dried. Last but not least, the nurse's hands, her dress, and her "droplets" need control.

In theory, control is simple. In practice, so far as implementation goes, control is very difficult. Obstruction is the main difficulty. It is so easy to say No ! Briefly, mattresses should be treated with warm moist vapourised formalin in the hospital steriliser or in a 'Sparkhall,' every time the bed has a new occupant. Mattress envelopes of rubber, plastic, or other enduring and impervious material will help. Pillows should be treated like mattresses. Blankets should be washed in 'Lissapol,' rinsed, centrifuged, and soaked in 'Fixanol C' every three weeks. Floor-dust will lie down under the 'O-Cedar' mop or the M.R.C. mixture of ninol, urea, and benzalkonium. Cups, &c., should be boiled after every meal in a large boiling-water steriliser. Nurses should wear thin rubber gloves, efficient masks, and efficient sterile overalls. If these simple measures were everywhere implemented the resistant microbial population of hospitals would very soon die out ; and these worrying infections be relegated to past history.

St. Margaret's Hospital, Epping, Essex. FRANK MARSH.

THE FINAL EXAMINATION

SIR,—Professor Bull (Aug. 25) states that the clinical part of the final examination shows near agreement between the examiners' marking. Surely, the clinical examination, where the candidates are in actual contact with patients, is the fairest and best way of testing their capabilities. I suggest that in the final examination in future the papers are not marked until the clinical results are known and that *only* those candidates who have not definitely failed in the clinical should have their papers marked. The system seems to be a good one since it would save the examiners work and candidates, who all know how important the clinical is, could still feel that they had failed justifiably even though their papers had

1. Colbeck, J. C. *Canad. Serv. med. J.* 1956, **12**, 563.
2. Boissard, J. M., Eton, B. *Brit. med. J.* Sept. 8, 1956, p. 574.

not been marked. Alternatively, the written papers could be held after the clinical part of the examination and only the candidates who have shown capability in the clinical need sit.

It seems rather anomalous that the clinical is allocated only 35% of the marks, as is done in Belfast at present, because a candidate who has done good papers, a good viva, and a poor clinical could be failed with a mark greater than 50%. I would think that the marks given to the clinical and to the papers should be reversed.

If the multiple-choice questions were to be substituted instead of the essay questions, the disadvantages of this type of questioning would be minimised and the final viva could still be used as a means of deciding about the candidate on the borderline.

It would be extremely interesting to read some final-year medical students' views on this subject.

London, W.12. J. D. W. WHITNEY.

SIR,—As an American student in a Netherlands university, I cannot comment on the British examining system. If, however, Dr. Tizard's suggestion of Sept. 22, concerning the preparation of a list of fifty questions and answers dealing with the recognition and treatment of medical emergencies, were to materialise as, for example, an article in *The Lancet*, I am sure it would be of service to many harassed medical students in their preparations for their examinations, as well as a benefit to the public.

While appreciating the many difficulties involved, I look forward to further action on this matter.

Leiden, Netherlands. S. DUBIN.

CLEFT PALATE FOLLOWING CORTISONE THERAPY IN EARLY PREGNANCY

SIR,—The paper by Mr. Harris and Dr. Ross,[1] describing a possible relation between cortisone therapy in early pregnancy and cleft palate, prompts us to record the following case.

A married woman was first seen in July, 1954, when she was aged 25. For three years she had had pain, swelling, and stiffness of some joints, anæmia, and Raynaud's phenomenon. Her symptoms were less during her first pregnancy. The baby was one month premature but otherwise normal. After this she had a long episode of fever with symptoms and signs of involvement of the heart and lungs. A clinical diagnosis of disseminated lupus erythematosus was made and treatment with cortisone and tolazoline started. Later L.E. cells were found in the blood. The patient became pregnant again while taking 100 mg. cortisone and 400 mg. tolazoline daily. The last normal period was on Sept. 23, 1955. Following an abrupt rise in weight, the membranes ruptured spontaneously on April 13, 1956; but labour did not start until seven weeks later. The baby was a male; he weighed 2 lb. 11 oz. and was thought to be more premature than the dates suggested. He died fourteen days later from bronchopneumonia. There was a cleft palate which involved the soft tissues; no other developmental abnormality was found on clinical or post-mortem examination.

This patient received a moderate dose of cortisone during the relevant period of development of the palate. A second patient with mild disseminated lupus erythematosus (joint symptoms and signs, butterfly rash, and L.E.-cell phenomenon) recently had a healthy baby who was born four weeks premature. During the first twelve weeks of her pregnancy, she was taking 10 mg. prednisolone daily (equivalent to 50 mg. cortisone). Of about 6000 deliveries in 1956, in the two obstetric hospitals concerned, these two patients are the only women who have received cortisone in early pregnancy and delivered a viable infant. A third patient with chronic hepatitis and a positive L.E.-cell phenomenon [2] received 50 mg. of cortisone during the first twelve weeks of her pregnancy. She had a therapeutic hysterotomy but no examination of the fœtus was made.

1. Harris, J. W. S., Ross, I. P. *Lancet*, 1956, i, 1045.
2. Joske, R. J., King, W. E. *Ibid*, 1955, ii, 477.

We mention these cases further to stimulate the interest roused by Mr. Harris and Dr. Ross and urge the reporting of the outcome of all pregnancies where the mother has taken cortisone in the first three or four months of pregnancy.

R. K. DOIG
Melbourne, Australia. O. MCK. COLTMAN.

PHENOXYMETHYLPENICILLIN IN PREVENTION OF RHEUMATIC FEVER

SIR,—We wish to record a possible disadvantage in the use of phenoxymethylpenicillin (penicillin V) in the prevention of further attacks of rheumatic fever.

When this substance became available, it was used in children with either active or inactive rheumatic fever to try to prevent further streptococcal infection. Treatment was carried out in one of the United Cardiff Hospitals which contains 24 beds reserved for the treatment of children with rheumatic fever. Each patient was given phenoxymethylpenicillin 125 mg. orally thrice daily under supervision from the day of admission. Weekly throat swabs were taken from each child.

Since the start of this scheme 35 children have received prophylactic phenoxymethylpenicillin. The throat swabs from 16 of these children showed β-hæmolytic streptococci of Lancefield group A, on at least one occasion.

In all, 134 swabs were examined from these 16 children. 38 yielded the organism, which was sensitive to 10 units of penicillin per ml. in 10, partially sensitive in 12, and insensitive in 14; the sensitivities of organisms from 2 swabs were not estimated.

2 children receiving regular phenoxymethylpenicillin developed a tonsillitis with hæmolytic streptococci in their throat swabs. Neither subsequently had any sign of activity of the rheumatic process.

In our experience phenoxymethylpenicillin, as given, has not eliminated β-hæmolytic streptococci of Lancefield group A in these children's throats, nor has it invariably prevented the development of tonsillitis.

An alarming feature was the frequency with which in-vitro penicillin-resistant strains were encountered. This suggests that the streptococcus may be following the staphylococcus in developing penicillin resistance. It would be interesting to know what experience others have had with this problem.

Departments of Pathology and Child Health, University of Wales, Cardiff. J. C. GRIFFITHS O. P. GRAY.

A RESIDENT'S COMPLAINT

SIR,—What can we expect from the Ministry of Health when we are let down by our own small units at hospital level? I asked for a return of emoluments while I was on holiday and was told that the Ministry would not allow this. I wrote as follows to the Minister:

"I have been able to arrange for a week's holiday and, on my return, I claimed a refund of the emolument for the period. I understand that it is the practice for the nursing staff of hospitals to be given some allowance in this respect. I was told that there was no refund payable to medical staff.

"The junior staff of the hospitals are already aggrieved by the conditions of their work. It is often impossible for them to get any holiday at all during their appointments. In this respect I have been more fortunate at this hospital. On the other hand it is hard enough for us to make ends meet without having our pay stopped for residence when we are on holiday.

"I feel sure that the ruling is not your own and I should be grateful for your support of my claim for a refund."

The Ministry's reply to this letter puts the matter squarely on to the local body:

"As you are no doubt aware, the Terms and Conditions of Service of Hospital Medical Staff state that 'a charge shall be fixed . . . equal to the value of the services provided.' Only the employing authority can say on what basis they fix the charge to a particular officer, i.e., whether in arriving at the annual charge they take into account the fact that the

officer will be on annual leave for a certain period. The decision as to a rebate must therefore rest with the employing authority.

"In the case of nursing staff the position is quite different, as the rates of charge laid down by the Whitley agreement are linked with a provision for rebates. Until there is some corresponding agreement in regard to medical staff the circumstances are not comparable."

With the last sentence I agree. The circumstances are not comparable. But they ought to be. And it seems to me time that the representatives of our profession gave a little more of their attention to the needs of their colleagues in residence.

Stockport. D. N. BARBER.

SEVERE DIPHTHERIA IN AN INOCULATED PATIENT

SIR,—It must be gratifying to all concerned with preventive medicine to see that a single classical case of faucial diphtheria is now so rare in this country as to merit publication. I would like to comment on some of the points raised by this report last week, by Dr. Winokur:

1. The case shows once again that antibiotics cannot make up for deficient administration of antitoxin. In such a case, at least 100,000 units antiserum should be given, preferably intravenously and in a single dose. Once toxin has been fixed to the target cells, as occurs in a long-standing case, divided doses are useless.

2. Diphtheria is a clinical and not a bacteriological diagnosis. Antitoxin must be given *before* swabbing is considered.

3. The patient reported cannot be regarded as being fully protected by inoculation when he developed the disease. It is well known that the initial immunity normally gained by a single inoculation gradually wanes so that after 5 years it is virtually non-existent. The fact that this child developed so severe an illness over $3^1/_2$ years after inoculation means that his immunity had fallen to almost nil, not that inoculation itself had failed to protect him. A booster dose which raises the immunity level to normal is usually given before starting school—i.e., at 5 years. It is unfortunate that this child was just too young to have received it.

Finally, a Schick test in February, 1956, when the child was first seen, would have been of interest, as it may well have been positive.

Ilford Isolation Hospital, Romford, Essex. I. M. LIBRACH.

TOXICITY OF FLUOROACETAMIDE

SIR,—The mode of action of fluoroacetate has been discussed by Peters and his co-workers,[1 2] who show that it is synthesised in vivo to fluorocitrate, the real toxic product, which blocks the tricarboxylic acid cycle at the aconitase stage. Peters[3] has given reasons for believing that C_2 compounds should reverse the above effect by supplying a depot of material from which citrate can be synthesised. Acetamide and other simple C_2 compounds do not, however, act antidotally, and this may be due to the very rapid conversion of fluorocitrate, so that there is no time for the C_2 compounds to compete. In other words, the conversion of fluoroacetate into fluorocitrate is probably much more rapid than that of acetate into citrate.

The position appears to be different with fluoroacetamide.

We have found that for two strains of laboratory rat the oral LD_{50} is almost exactly 15 mg. per kg., compared with 1·2 mg. per kg. for sodium fluoroacetamide, and the LD_{100} 19–20 mg. per kg. Bentley[4] has recently reported a similar LD_{50} for fluoroacetamide in the case of the wild brown rat, *Rattus norvegicus* Berkenhout, 1769. Animals poisoned with fluoroacetamide lie on their sides or in a huddled position, and exhibit convulsive spasms on being touched. When acetamide is added in the ratio of 4 : 1 or 9 : 1 parts fluoroacetamide, the onset of symptoms is delayed and the LD_{50} of the fluoroacetamide itself is increased to between 25 and 30 mg. per kg. Sodium acetate does not have a similar effect, but *l*-cysteine hydrochloride is as active as acetamide.

Acetamide is also an effective antidote to fluoroacetamide if used sufficiently rapidly, and, administered by mouth at a rate of 200 mg. per kg., will prevent fatalities when given 30–40 minutes later in the case of 35 mg. per kg. and up to 65 minutes later following doses of 20 mg. per kg.

The cumulative effect of fluoroacetamide cannot be very great, for we have fed rats 3 mg. per kg. daily for 20 consecutive days without harm. At this dosage level, at least 60% of the fluoroacetamide is excreted unchanged in the urine.

It has been shown by Anker and Raper[5] that acetamide is not converted rapidly to acetic acid in vivo, and it is probable that fluoroacetamide is similarly converted slowly to its corresponding acid and is therefore of a relatively lower order of toxicity.

In view of the above considerations, and of the fact that solutions containing 1% and 2% *w/v* fluoroacetamide have not been found to give off detectable fluoroacetamide into the atmosphere, even at 45°C, it may be concluded that fluoroacetamide is a much safer substance to handle than either sodium fluoroacetate or the fluoroacetic esters.

Romford. M. A. PHILLIPS.

Nutritional Research Unit, Huntingdon. ALASTAIR N. WORDEN.

POLIOMYELITIS AND THE SEASONS

SIR,—Poliomyelitis, as notified weekly to the Registrar-General for England and Wales, shows a fairly regular annual peak at the end of August or early September. This has been noted by many other observers, and is now an accepted characteristic of the disease. (In the years when the peak occurred somewhat later a probable explanation is that earlier cases had been missed, or had been labelled "summer influenza.") The English summer, however, is capricious, and meteorological records over the years do not show the same annual consistency. I think that it is unlikely that the weather is itself responsible for the regular rise at this specific period.

Many factors obviously influence the epidemiology of the disease, and I should like to stress several points which I have noted over the post-war years. As a field-worker, I visit numerous cases and their contacts. For six years I worked in an area where camping is widespread, the majority of the campers being parties of school-children and of adolescents belonging to various youth organisations. In such camps the food preparation and the cooking is usually done by the campers themselves, taking turn and turn about.

When investigating poliomyelitis in these camps, I usually found that close interrogation of contacts was highly rewarding. For every confirmed case occurring in a camping party, one could expect to find up to half a dozen abortive and mild non-paralytic cases, the number varying with the size of the group and the length of time they had been camping together.

Now, I believe very firmly in the important part played by faecal contamination in the spread of this disease in a community. As a realist, I do not believe that more than 10% of the population is careful about hand-washing after defæcation (even when free facilities are available, as they are in this city). Perfunctory dipping of the fingers in cold water is unlikely to remove infection from those fingers.

Regularly each August, many thousands of young vulnerable persons live together in groups, either under canvas, or in schools or church halls. After one, two, or three weeks they return to their homes. If one accepts that the intestine remains infective for up to six weeks after the initial infection and that the incubation period is about six to ten days, it is not surprising that the national peak should occur at the end of August or early September, as a result of large numbers of recently infected (though symptomless) young persons returning to their families.

Those of us who have experience of such camps will agree that the facilities for personal hygiene are either inadequate or are not used as they might be. Living "rough" is not conducive to personal cleanliness even amongst the minority

1. Peters, R. A., Wakelin, R. W., Buffa, P., Thomas, L. C. *Proc. roy. Soc.* B. 1953, **140**, 497.
2. Gal, E. M., Peters, R. A., Wakelin, R. W. *Biochem. J.* 1956, **64**, 161.
3. Peters, R. A. *Endeavour*, 1954, **13**, 147.
4. Bentley, E. W. *Sanitarian*, July 1956, p. 392.
5. Anker, H. A., Raper, R. *J. biol. Chem.* 1948, **176**, 1353.

who are fastidious about hand-washing at other times. When water has to be man-handled any distance, the temptation to let hygiene go by the board is perhaps understandable.

No, Sir! I suggest that it is not the weather, but rather the season, which influences infection-rate. If school holidays were to start a month earlier, then it is not unlikely that the national peak of infection would be correspondingly earlier.

Public Health Department, Chichester. D. WARREN BROWNE Medical Officer of Health.

INSULIN-NEUTRALISING ANTIBODIES

SIR,—With regard to your annotation (Sept. 1), serologic antibodies against insulin detected by a complement-fixation reaction were first reported in 1937 by J. Bauer, E. Kunewaelder, and F. Schächter [1] and J. Bauer.[2] The appearance of these antibodies produced experimentally in rabbits was not associated with a higher resistance of the animals against insulin. Three patients with spontaneous hypoglycæmia, one with a proved insuloma of the pancreas, also gave a positive complement-fixation with insulin as antigen.

Los Angeles, California, U.S.A. JULIUS BAUER.

ARTIFICIAL HIBERNATION IN HEART-DISEASE

SIR,—Some time ago we recommended administration of the "lytic cocktail" (chlorpromazine, promethazine, and pethidine in a ratio of 1 : 1 : 2) for promoting diuresis in patients with œdema of cardiac origin.[3] We have found that the mixture offers considerable advantages in three further fields of cardiology.

1. *Supraventricular paroxysmal tachycardia* is mostly of nervous origin. Wherever the impulse giving rise to the attack originates, the underlying factor is adrenergic excitation. All methods hitherto recommended for relieving the condition (pressure on the orbits, digitalis, acetylcholine, &c.) are based on excitation of the parasympathetic. We thought that drugs decreasing adrenergic activity might be better suited to the purpose.

Three patients with supraventricular paroxysmal tachycardia were therefore treated with a small dose of the lytic cocktail; a total quantity containing 0·3–0·6 mg. of chlorpromazine per kg. of body-weight was administered intravenously in two equal doses, within twenty minutes. Relief was almost instantaneous. The "cocktail" seems preferable to chlorpromazine alone, since this drug may in certain cases enhance tachycardia. Treatment with digitalis or strophanthin constitutes no contra-indication.

To prevent the paroxysmal attacks by ensuring protracted inhibition of the sympathetic nervous system, we have prescribed 0·1 mg. of reserpine t.i.d. for children, and 0·15 mg. t.i.d. for adults. On this régime two patients, who had been having three or four attacks every week, and a third patient with as many as eight to ten attacks daily, were relieved after a few days of treatment, and for several months now they have not had an attack. In our experience, reserpine is excellently suited for relieving tachycardia of nervous origin in children. A daily dose of 0·1 mg., which in our patients has not influenced blood-pressure or caused side-effects, is recommended for this purpose.

2. *Cyanotic attacks in "blue babies"* are, in our opinion, due to spasm of collateral arteries. In these most dangerous episodes the "lytic cocktail" represents a life-saving measure. The dose for this purpose is again an amount containing 0·3–0·6 mg. of chlorpromazine per kg. of body-weight, injected intravenously in two equal doses at an interval of twenty minutes.

3. *Angiocardiography.*—We have successfully used doses of the "lytic cocktail" incorporating up to 1 mg. per kg. of chlorpromazine at angiocardiography. Much smaller doses ensure perfect sedation, and protection against undesirable complications. But the patient must still be tested for sensitivity to iodine. Administration of the cocktail is naturally contra-indicated before cardiac catheterisation, since it greatly alters pressure conditions in the blood-vessels.

1st Department of Paediatrics, Budapest University Medical School. J. SZUTRÉLY P. V. VÉGHELYI.

1 *Wien. Klin. Wschr.* 1937, **50**, 83.
2. *J. Amer. med. Ass.* 1937, **109**, 1442.
3. Szutréiy, J., Véghelyi, P. V. *Lancet*, 1956, i, 205.

PSYCHOTHERAPY IN ULCERATIVE COLITIS

SIR,—I am grateful to Dr. Ambrose (Aug. 11) for his suggestion that hypnosis is of value in ulcerative colitis where there is resistance by the patient to a release of emotional problems. I can imagine it might be life-saving in a few fulminating cases. However, I do not see this method replacing normal interviews, as insight, which must be the ultimate goal, is acquired only slowly by most patients.

X.Y.Z. (Aug. 18) raises several interesting points to which space forbids a detailed reply. I agree with him that the ideal situation to be sought is complete independence of the sufferer—independence from mother, mother-figure, father, and *doctor*. Unfortunately most people cannot achieve this without help. Occasionally one meets a person with intelligence and insight who listens, goes away, and solves his own problem. I have a Christmas card every year from just such a person. Some persons stand up for themselves very well in one sphere, but not in another. Many of my patients went through the war as combatants, and I have heard of a boxer with the disease.

Finally, may I correct an omission in my paper by drawing attention to the article by Groen and Bastiaans.[1] They were the first to record a follow-up of the results of psychotherapy in colitis, having studied 29 cases for one to ten years.

Ipswich. J. W. PAULLEY.

UNDESCENDED TESTIS

SIR,—It may be of interest that the East Anglian branch of the Society of Medical Officers of Health, through their research committee, are at present investigating the prevalence of unilateral and bilateral undescended testicles in age-groups in boys attending local-authority schools in East Anglia. It is hoped to demonstrate the size of the problem, and it may be possible to comment upon the age of application and the result of treatment.

P. A. TYSER
President, East Anglian Branch, Society of Medical Officers of Health.
Cambridge.

RENAL INFARCTION WITH HYPERTENSION

SIR,—The article by Dr. Hunter and Dr. McElmoyle (Sept. 1) contained no references, and perhaps left the impression that the case reported was a unique experience. Because of the great significance that must be attached to the findings reported here and elsewhere in similar situations, it would seem valuable to comment on the association between hypertension and unilateral renal disease of vascular origin.

There are numerous examples of the Goldblatt phenomenon occurring in man. Particular interest has been shown recently in the possibility of less overt vascular causes of renal hypertension, and attempts to diagnose these instances have met with considerable promise. The efforts of Dr. John Eager Howard of the Johns Hopkins Hospital have been notable in this respect, and his technique has been successful in selecting cases where pyelography and dye studies were essentially normal. This procedure consists of bilateral ureteral catheterisation and estimation of the water and sodium excretion of each kidney. In most instances of unilateral disease on a vascular basis, the affected side has shown more than 50% difference in the excretion of water, and at least 15–20% reduction in sodium concentration.[2 3] The demonstration of decreased size of the affected kidney is final confirmation, and, if possible, all three criteria should be satisfied before operation.

The importance of these observations is readily appreciated when one considers the tremendous potential

1. Groen, J., Bastiaans, J. *Gastroenterology*, 1951, **17**, 344.
2. Howard, J. E. *Amer. J. Obstet. Gynec.* 1954, **68**, 1212.
3. Howard, J. E., Connor, T. B. *Trans. Ass. Amer. Physns* (in the press).

salvage-rate, and the comparative ease of the diagnostic procedure referred to. It should be emphasised that symptoms referable to the urinary tract are often absent in this condition, although a previous history of sudden flank pain and/or hæmaturia is certainly suggestive, and not uncommon. This represents a radical departure from the dictum that "a unilaterally diseased kidney in a hypertensive patient should not be removed unless there exists some indication for its removal in addition to the hypertension." [4]

San Antonio, Texas, U.S.A. PAUL J. ROSCH.

DISMISSAL ON MEDICAL GROUNDS

SIR,—May I, as a health visitor working with tuberculous patients, comment on Dr. Todd's letter (Sept. 1)? Dr. Todd appeals for a more realistic approach to the needs of persons seeking employment on recovery from injury or illness of long standing.

It is encouraging to those of us who meet persons facing these problems to find a doctor with courage pointing out the hardship and, indeed, injustice suffered by many. On the face of it the only reason for the "medical" is to assure the employing authority that a prospective employee will not become a liability on the superannuation scheme before reaching the latest possible retiring age.

While the solvency of superannuation schemes is important to those of us who will need to depend on them when we come to retire, it is unfortunate that (to mention only those public bodies within our own orbit) Ministries, local authorities, hospital authorities, and banks regularly refuse training and employment to young people and others whose only disadvantage is that they have had pulmonary tuberculosis. The fact that they have recovered is not considered.

Could we, who are interested, campaign for a more generous attitude? The examining doctor has a great deal of authority as well as responsibility and could do much to help overcome this stumbling-block.

Would an alternative pension scheme for certain special cases be an advantage—something in the nature of an endowment policy which could only be surrendered at pension age or on previous retirement through illness? In this way the, often wrongly, anticipated burden on ordinary pension schemes would be avoided and the employee given some safeguard for his future.

SUPERINTENDENT HEALTH VISITOR.

TREATMENT OF ACUTE PANCREATITIS WITH CORTISONE

SIR,—It is strange that so little attention has been paid to the rôle of the adrenal glands in acute pancreatitis. The standard surgical and pathological texts emphasise the œdema and necrosis, which often extend some distance from the pancreas itself, but do not mention involvement of the adrenal glands by the inflammatory process.

The left adrenal gland is in direct contact with the tail of the pancreas, and on the right side the head of the pancreas is separated from the adrenal gland by only a very small amount of retroperitoneal tissue. In fatal cases of acute pancreatitis examined post mortem the adrenals are not infrequently found surrounded by inflamed necrotic tissue. It would not be surprising if, in these circumstances, there were some disturbance of adrenal function.

The severe shock in patients with this condition is well recognised. It may well be that the beneficial results of treatment with cortisone, described last week by Mr. Rogers and his colleagues, are due to the drug's supportive action during a period of temporary adrenal failure.

Wolverhampton. ALLAN JACOBS.

4. Green, D. M. *In* Third Annual Report on Stress. Edited by H. Selye and A. Horava. Montreal, 1953; p. 277.

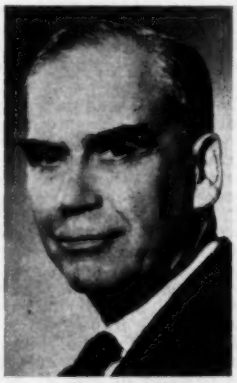
Obituary

WILLIAM GILLIATT

K.C.V.O., M.D., M.S. Lond., F.R.C.P., F.R.C.S., F.R.C.O.G., Hon. M.M.S.A.

THE death of Sir William Gilliatt after a road accident on Sept. 27 brings to a tragic end a life-time of service to his patients and to our profession.

He was born at Boston in Lincolnshire in 1884, and entered the Middlesex Hospital for his medical training. During his distinguished career as a student he won the Hetley scholarship, the junior Broderip scholarship, the Hudson scholarship, and the Lyell gold medal. After qualification in 1908 he held the posts of house-physician, house-surgeon, obstetric house-physician, and obstetric and gynæcological registrar and tutor at the Middlesex. By 1912 he had acquired the degrees of M.D. (with the gold medal) and M.S., and also the F.R.C.S. He was evidently a man of high promise, marked out for a consultant career at a time when competition was more open, and also perhaps more difficult, because there was then no fixed pattern of training. The Middlesex school had a high reputation for gynæcological surgery, founded on the work of Bland-Sutton, Victor Bonney, and Comyns Berkeley, and Gilliatt had the good fortune to be trained in this tradition. There was no vacancy on the staff of the Middlesex, and it proved to be to the great gain of King's College Hospital when he was appointed assistant obstetric and gynæcological surgeon there in 1916. He became full surgeon in 1925, and remained at King's until he reached the age of retirement in 1946, when he was appointed consulting surgeon. His services to King's continued until his death, for he later became vice-chairman of the board of governors and chairman of the medical school council, and to these tasks he brought the same wise care and enthusiasm as he had shown in his clinical work. As chairman of the nursing committee the welfare and education of the nurses became his particular interest.



[P.A.—Reuter Photo

Gilliatt was also appointed obstetric physician (as the title then was) to Queen Charlotte's Hospital, and surgeon to the Samaritan Hospital, and he served as consultant surgeon to Bromley Hospital, the Maudsley Hospital, and St. Saviour's Hospital.

Gilliatt was an excellent clinical teacher. His outpatient clinic and his ward rounds were always attended by a crowd of students, in spite of the hazard of his invariable method of asking questions round the class, from which there was no escape and which soon exposed the ignorant. His outstandingly good judgment and his gift for seizing upon the essential point of any subject or clinical problem were the secrets of his success. His skill, quiet authority, and charm of manner brought him a large private practice, and this was augmented as his students qualified and not only sent to him their patients but their wives, and many an old King's man owes "Bill" a debt both for his teaching and for advice to his family. He was a real consultant, and his help was not infrequently sought by other obstetricians in particularly difficult cases.

The time came when he was called upon to undertake the responsibility of advising the Royal Family. After attending the Duchess of Kent at the births of her three children, he attended the Queen (then Princess Elizabeth) at the birth of the Duke of Cornwall in 1948 and of Princess Anne in 1950. But even when his practice was large and his responsibility was great he always found time for his hospital work, and old patients still attend who refer appreciatively to their treatment by "Mr. Gilliatt," and who seem to gain satisfaction and some reflected glory from his subsequent promotion.

He rendered great services to the Royal College of Obstetricians and Gynæcologists, of which he was a foundation fellow, and he served on the council from 1932 until his death. He was honorary secretary in 1942 during the difficult days of the war, and he became president in 1946. In this high office his courtesy, dignity, and sincerity more than made up for an initial slight diffidence in public speaking, but he quickly overcame this difficulty. There is not space here to list the innumerable professional committees on which he served, on many of them at a time when the future of the profession under the National Health Service was under discussion. His good will, high ability, and strong personality made him an effective member of any committee; and indeed in any committee the chair often seemed his natural place.

He was appointed C.V.O. in 1936, and promoted K.C.V.O. in 1949, but his knighthood only seemed to make him more modest, and it was characteristic that when he was appointed surgeon gynæcologist to the Queen in 1952 he told a close friend that he regarded this as an honour to the Royal College as much as to himself. He was elected president of the Royal Society of Medicine in 1954, and he greatly appreciated this sign of the esteem of his profession.

Gilliatt was not a tall man, but his fine head gave him a good presence, and he appeared many years younger than his age. In ordinary conversation he spoke briefly, probably because he thought carefully before speaking, and sometimes he gave the impression that he was a little shy. His influence on his housemen was probably greater than he or they realised at the time. To telephone to him or to consult him about a case was itself educational, for he had an unerring knack of discovering any neglect in examination or treatment, although he seldom made any direct criticism. He was fortunate in having great self-confidence, and yet there was much humility in him, and in later years he would not hesitate to seek advice even from his juniors on some point of technique on which he thought—often wrongly—that he was not up to date. As a surgeon he was painstaking and utterly reliable, but never a brilliant "technician." His simple and effective methods were easily transplanted to nursing-homes in which much of his private work had then to be done, and he never depended on elaborate teams of assistants.

Sir William wrote relatively little in the medical journals, but his influence on obstetrical and gynæcological practice was considerable, largely through his many friendly contacts with other gynæcologists. In particular he was an early champion of the lower-segment cæsarean operation, and he demonstrated its safety even late in labour many years before antibiotics were available. He was a regular contributor to the *Ten Teachers* textbooks, and examined for several universities and the Conjoint Board.

This brief and bare account of Sir William Gilliatt's achievements may fail to convey to those who never met him the charm and sincerity of this quiet man, who was so widely liked and respected. He was not easily approachable, yet he never failed to give kind and frank advice on any professional matter to those, whether junior or senior, who sought his help. Perhaps the simple words of the Duke of Edinburgh sum up our feelings about him: "He has been a great help to my family." In no less degree Gilliatt has helped his patients, his students, and his colleagues.

S. G. C.

William Gilliatt's long association with, and distinguished service to, the Royal College of Obstetricians and Gynæcologists rates him as one of the very great men in the history of the college. He was a founder fellow, 27 years ago, and even at that time, so great were his personal prestige and professional attainments that he was early invited to take an active interest in college affairs—an interest that never waned throughout the rest of his life.

He assumed the presidency in 1946 at a difficult time in the college history. The war had ended, and the many negotiations before the introduction of the National Health Service fell to his lot. He always expressed dissatisfaction at the outcome of the negotiations for the national maternity service. It was during his presidency, too, that the Royal Charter was granted to the college, and in 1947 he admitted Field-Marshal Jan Smuts to the honorary fellowship. With the then honorary treasurer, now Sir Arthur Gemmell, he renewed the appeal effort for the building of the new college in Regent's Park by invoking the help of Sir Ronald (now Lord) Weeks, as appeal chairman. It is a matter of regret that he has not lived to see the laying of the foundation stone next year.

Sir William's unique association with our Royal Family could not other than influence their interest in our college. In 1949 the Queen (then Princess Elizabeth) and the Duke of Edinburgh attended our annual dinner under his chairmanship. Queen Elizabeth the Queen Mother also accepted the office of patron of the college and the honorary fellowship, and Sir William performed the ceremony of admission at the very end of his presidency in 1949. This was made possible by a generous gesture on the part of his successor, Dame Hilda Lloyd, who postponed her own admission to office to enable Sir William to admit our patron to the honorary fellowship, and afterwards to administer the oath to his own successor.

Few accomplish so much during a term of three years as president; but William Gilliatt shirked nothing, and even after the end of his presidency his interest in the college and its influence for good remained foremost in his thoughts. We will miss his wise counsel, his shrewd judgment, his kindliness and helpfulness, and his outstanding common sense. I personally will miss, more than I can say, the friendship of a man of integrity, whose willingness to help at all times will ever be remembered and appreciated.

C. D. R.

He married Dr. Anne Louise Kann, who was senior anæsthetist to the Royal Free Hospital. She survives him with a daughter and a son who is physician to the National Hospital, Queen Square.

DOUGLAS ALFRED LANGHORNE

M.B.E., T.D., F.R.C.S.E.

Mr. D. A. Langhorne, surgeon to the Royal West Sussex Hospital, Chichester, died on Sept. 20 at the age of 51. He was born at Bennington, Hertfordshire, and qualified from St. Bartholomew's Hospital in 1927. He held house-appointments at Barts before he became assistant in plastic surgery under Sir Harold Gillies, and in 1930 he took the F.R.C.S.E. Soon afterwards he settled in general practice with Dr. A. H. Bostock at Chichester, but surgery remained his chief interest and he was appointed to the staff of the Royal West Sussex Hospital as assistant orthopædic surgeon. He was later appointed surgeon to the Royal West Sussex Hospital and also to the Royal West Sussex County Mental Hospital.

He was an enthusiastic and conscientious Territorial Army officer, and during the war he served in Iceland and later on the Burma front. His courage and hard work in the Imphal pocket during the six months of the siege will be remembered with gratitude by the wounded, and for this service he was appointed M.B.E. After the war, he decided to give all his time to surgery and he retired from his partnership in general practice.

"Langhorne's interests outside his profession," writes H. T., "were many and diverse. He was fascinated by the natural history of birds and was a keen birdwatcher. He was interested in archæology, was a painter of merit, and a keen yachtsman. While he was in Iceland he wrote an attractive book on the natural beauties of that country. In the Chichester community he gave much of his time to voluntary organisations. He was a handsome, friendly, gay man, with a balanced philosophy of life and an innate modesty, and he was loved by all who knew him."

Mr. Langhorne leaves a widow and three sons.

DERYCK RALPH SYRED
M.R.C.S., D.M.R.

Dr. Syred, a consultant radiologist to Northampton General Hospital, died on Sept. 19 after a short illness. He was born at High Wycombe and educated at Caterham and at St. Bartholomew's Hospital. He qualified in 1940, and with just over a year's hospital experience he joined the R.N.V.R. in 1941. His destroyer was torpedoed in the second battle of the Java Sea, and after twenty-four hours in the water he was picked up by the Japanese, in whose hands he remained a prisoner-of-war for over three years. His native ingenuity was taxed to improvise and extend his miserable medical supplies to the utmost benefit of his fellow prisoners, but his work for them under difficulty earned a mention in despatches. After he was demobilised he was trained in radiology at the Middlesex Hospital, taking the D.M.R.D. in 1948. He then went to Northampton as senior registrar, and since 1951 has held a consultant radiodiagnostic appointment with the Northampton and Kettering hospital groups.

G. H. writes: "Dr. Syred's work was characterised by diligent application to detail, and careful questioning appraisal of clinical problems. His prisoner-of-war experiences had left their mark, but his assurance and confidence were gradually restored, reflecting the increasing respect shown for his opinion. His main outside interest was sailing—with swimming as a necessary associated accomplishment. We shall remember him for his sincerity, his hard work, his quiet charm, and occasional gay outbursts of laughter."

He leaves a widow, two sons, and a daughter.

WILLIAM CUTHBERTSON
M.B. Glasg.

Dr. Cuthbertson, who died on Sept. 19 at his home in Leyton, Essex, at the age of 59, studied medicine at Glasgow University. Soon after qualifying in 1924 he joined partnership with a fellow Scot and ran a busy general practice in Walthamstow, Leyton, and Woodford, and during the war years he ran it single-handed. For many years he was honorary physician to the Walthamstow Child Welfare Society. N. A. T. writes: "Cuthbertson was a practising Christian and a good man in the true sense of the word. He always put his duty to his patients before his personal convenience. I knew him for almost thirty years both as a patient and later as a colleague and I am sure that his patients have lost a tireless friend and comforter as well as a competent general practitioner."

Dr. Cuthbertson leaves a widow, a son who is a final-year medical student, and a daughter.

Appointments

BLUMBERG, N. A., M.B. Witw'srand, F.R.C.S.: surgical registrar, Ipswich and East Suffolk Hospital.
EVANS, G. P. A., M.B. Glasg.: assistant M.O.H., Walsall.
LOGUE, VALENTINE, M.B. Lond., F.R.C.S.: consultant neurosurgeon, Middlesex Hospital, London.
PRIEST, ELIZABETH A. F., M.B. Aberd., M.R.C.P.: whole-time assistant cardiologist, Aberdeen general hospitals.
SMITH, S. B. S., L.M.S.S.A., D.T.M. & H.: assistant M.O.H. and principal school M.O., Swindon.
WIGLEY, MARGARET D., M.B. Birm., D.C.H.: assistant M.O.H., Walsall.
YOUSUF, S., M.B., D.A.: anæsthetic registrar, Ipswich and East Suffolk Hospital.

Birmingham Regional Hospital Board:

CAPE, R. D. T., M.D. Edin., M.R.C.P.E.: whole-time consultant gerontologist, Birmingham (Selly Oak) group of hospitals.
CHAPLIN, A. E., M.D. Birm.: whole-time consultant pathologist, Birmingham (Dudley Road) group of hospitals.
EVANS, ROBERT, M.D. Belf., F.R.C.S., D.L.O.: part-time consultant E.N.T. surgeon, Mid-Worcestershire group of hospitals.
FISHER, H. J., F.R.C.S.E., M.R.C.O.G.: part-time consultant obstetrician and gynæcologist, Wolverhampton group of hospitals.
HUTCHINSON, J. A., M.B. Birm., D.P.M.: whole-time assistant psychiatrist, North Staffs (mental A) group of hospitals.

Colonial Appointments:

BASU, K. M., M.B. Calcutta, M.R.C.P.I.: M.O., Gold Coast.
DALBY, M. A., M.D. Copenhagen: M.O., Gold Coast.
HAMILTON, H. F., M.B. Edin., M.R.C.P.: junior physician, medical department, British Guiana.
MCCORMACK, KEVIN, M.B. N.U.I.: M.O., Tanganyika.
MASSIAH, V. I., M.B., N.U.I.: M.O., grade B, Trinidad.
NORDSTED-JORGENSEN, A. E., M.D. Copenhagen: M.O., Gambia.
PHILLIPS, L. A., M.B. Lond., D.A.: M.O. (anæsthetist) S.P.H.S., Fiji.
SEMPLE, J. A., M.B.: senior M.O., St. Kitts Nevis and Anguilla, Leeward Islands.
SLADE, M., M.R.C.S.: health officer, Brunei.
STORE, F. R., M.R.C.S.: M.O., Cyprus.

Notes and News

HYOSCINE IN EYE-DROPS

ON Sept. 20 six children who attended a clinic at Twickenham were given eye-drops before an ophthalmic examination. Soon afterwards the children became hallucinated and disorientated and they were taken to hospital. A statement[1] issued last week by the Middlesex County Council said that five of the children had fully recovered and the sixth was progressing satisfactorily. The prescription for the eye-drops was homatropine hydrobromide 2%, cocaine hydrochloride 2%, boracic acid 1%, all in distilled water. The results of an analysis disclosed that apparently hyoscine hydrobromide was used instead of homatropine. The children's symptoms were consistent with the analyst's findings, the statement added. "The question of the error in the dispensing in the prescription is being taken up with the firm of chemists who made the prescription."

University of London

Dr. W. F. Widdas, senior lecturer in physiology at King's College, has been appointed to the university readership in physiology at the college.

University of Leeds

At recent examinations the following were successful:

M.D.—J. K. Walker.
M.B., Ch.B.—Dulcie L. Atwell, A. C. Bastin, D. G. Beeton, A. E. Biggin, J. R. E. Bishop, Pavils Cakuls, John Clarke, J. H. Danby, D. V. Denton, E. D. J. Diaper, Bandele Odunayo Faschun, M. D. Hargreaves, F. G. Harris, Alexander Haskell, Pamela J. Heatley, Ignace Hee Seong KooSeenLin, Thomas Kraft, D. A. Marshall, B. C. Nkemena, P. B. Odgers, Willie Priddy, J. L. Ramsay, R. W. Richardson, Leslie Stankler, Ann Stockwell, Geoffrey Taylor, J. D. Walker, Howard Watson, Harry Welsh, J. H. Winder, Mabel Yates.

University of Liverpool

Prof. Bryan McFarland is to deliver the first McMurray lecture in orthopædic surgery on Tuesday, Nov. 20, at 5.15 P.M. in the arts theatre of the university. He is to speak on the life and work of Thomas Porter McMurray.

Teaching Backward Children

On Oct. 20 the Guild of Diploma Teachers of Backward Children will publish the first issue of their journal *Forward Trends in the Treatment of the Backward Child*. Further particulars can be had from Mr. S. S. Segal, hon. secretary to the guild, 10, Fielding House, Boundary Road, St. John's Wood, London, N.W.8.

Middlesex Hospital Medical School

A start will be made early in the New Year on the building of the new medical school and residential college for the Middlesex Hospital. Speaking of these plans at the school's annual dinner on Sept. 28, Prof. B. W. Windeyer, the dean, announced that their accomplishment had been brought much nearer by the generosity of Mr. Edward Lewis, an old friend of the hospital and chairman of Decca Radar Ltd. Mr. Lewis had covenanted in terms that would provide more than £122,000 over the next seven years. At last year's dinner Professor Windeyer announced the gift of £400,000 from Colonel J. J. Astor (now Lord Astor of Hever) towards the rebuilding of the medical school; and this year Mr. F. W. Roques, who was in the chair at the dinner, spoke of Lord Astor's long and hard work for the Middlesex, for the past 18 years as chairman of the hospital. There was warm applause when Mr. Roques congratulated Lord Astor on the well-merited honour of barony which he had received in the past year. Proposing the Middlesex Hospital and Medical School, Mr. Roques also referred to the three new Middlesex knights of the past year—Sir Samuel Bedson, F.R.S., Sir Tudor Thomas, and Sir Victor Negus. In able support of Professor Windeyer's reply, Dr. L. G. Whitby, senior Broderip scholar, looked forward to a more rewarding corporate life for students when the new buildings were ready; but of present-day student affairs he was less sanguine. He spoke ruefully of fireworks at fever hospitals and he seemed to have detected occasional lapses from decorum which might, he feared, lose students some of their privileges. Proposing the chairman's health, Mr. E. W. Riches commented on the Middlesex tradition of exporting obstetricians and gynæcologists; but Mr. Roques had clearly been "too expert for export."

1. *Times*, Sept. 27, 1956.

Royal College of Obstetricians and Gynæcologists

At the meeting of the council held on Sept. 28, with Mr. Charles D. Read, the president, in the chair, Viscount Nuffield and Lord Weeks were admitted to the honorary fellowship.

The following were admitted to the membership:

L. Allan Allen, Arthur Bates, R. G. Blair, G. L. Bourne, Nancy I. Cardno, Emanuel Cassar, William Chanen, P. A. Deck, Jan Naudé de Villiers, Meenakshi Ghosh, J. P. Hendrickse, B. M. Hibbard, David Howell, R. A. St. C. Hoyte, Elsie S. Jaikaran, P. J. Joubert, A. M. Kelso, A. W. Laughland, D. W. Leslie, Cecilia M. Liggins, G. C. Liggins, E. M. Little, J. D. O. Loudon, P. C. McAuliffe, Clara J. McFarlane, Marion C. Miller, Sachindranath Nan, W. J. O'Sullivan, S. W. Fitz-Patrick Page, J. K. P. Perera, Shephalika Prodhan, N. A. Regan, Kathleen J. Rennie, Philip Rhodes, D. W. T. Roberts, I. D. Ronayne, A. O. Sankey, H. H. A. Sauer, Teddy Schneider, J. S. Skipper, T. S. Train, N. W. F. Weir, A. J. Woolf, Janet W. Worling.

In proposing the toast of The College at the annual dinner on Sept. 28, Mr. R. H. Turton, the Minister of Health, paid tribute to the part that Sir William Gilliatt had played in reducing infant mortality in this country. But, though great progress had been made in the past fifty years, Mr. Turton confessed himself still dissatisfied, especially with the mortality of infants in the first week of life and with the stillbirth-rate. The Government had lately set up the Cranbrook Committee to survey the maternity services of the nation and he was anxious to have its report as soon as possible. Mr. Charles Read, the president, replying for the college, expressed his pleasure and surprise that twelve months' close coöperation with the Minister and his medical officers had convinced him that these people were both human and amenable to reason. The evidence which the college was submitting to the Cranbrook Committee was substantially the same as the report on the maternity services which the college had issued in 1954. Reporting on the past year in the college, Mr. Read said that a regional council had been inaugurated in South Africa last July. Progress had also been made with the preparations for the new college building on the Regent's Park site, and it looked as though the foundation stone would be laid next year. Enough money had been collected for the building. In the next three years they must collect enough capital to maintain the college, and he was glad to announce that they would receive a substantial legacy under the will of the late Donald Stafford Matthews and that he had that morning been offered a donation of £10,000 in memory of Sir William Gilliatt.

Prof. T. N. A. Jeffcoate in toasting The Guests explained that the phrase had its origin in the spiced sippet which used to lurk at the bottom of the glass. Turning into a hospitable crystal-gazer he accordingly invited the company to look into the depth of their glasses and there he found for them Mr. Turton, Sir John Charles, Dr. Kenneth Cowan, and Lord Nuffield. The guests, Professor Jeffcoate pointed out, also included such a wealth of skilled helpers—anæsthetists, radiologists, psychologists, and midwives—that he sometimes wondered if delegation was not a more serious threat to the obstetricians' livelihood than automation. Indeed he had heard rumours of the nationalisation of the birth canal and if so who should pilot the passenger through? He understood that all the unborn children were already banding themselves together to form a canal users' association. Mr. Dickson Wright, president of the Medical Society of London, replied for the guests.

André Mayer Fellowships

These fellowships, named after the late André Mayer, will be awarded by the Food and Agriculture Organisation of the United Nations to persons with high qualifications who have shown aptitude for research and who would benefit from additional training.

Five or six fellowships will be offered in 1956 and will be spread over the whole field covered by F.A.O.—i.e., agriculture, agricultural economics and statistics, fisheries, forestry, and nutrition. Awards will be given for up to two years, with possible extension up to thirty months, and payment is expected to be at the rate of $250 a month. Further information may be had from the secretariat of the F.A.O. National Committee for the United Kingdom, c/o Ministry of Agriculture, Fisheries, and Food, 10, Whitehall Place, London, S.W.1.

St. Thomas's Hospital

The old students' dinner will be held at the Royal College of Surgeons, Lincoln's Inn Fields, London, W.C.2, on Thursday Nov. 8, at 7.30 P.M. Prof. A. D. Gardner will be in the chair. Tickets (£1 11*s.* 6*d.*) may be had from the beadle to the medical school.

Royal Eye Hospital

This hospital has been transferred from the King's College Hospital group to the South West Metropolitan Regional Hospital Board.

Kettle Lecture

Dr. A. H. T. Robb-Smith will deliver this lecture at the Wright-Fleming Institute, St. Mary's Hospital Medical School, London, W.2, on Friday, Nov. 30, at 5 P.M. He will speak on inflammation and infection.

CORRIGENDUM: *New Pathways in Cellular Metabolism.*—This title was incorrectly applied last week (p. 662) to Prof. G. R. Cameron's new book, which in fact is called *New Pathways in Cellular Pathology.*

Diary of the Week

OCT. 7 TO 13

Monday, 8th

POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road, W.12
4 P.M. Dr. E. G. L. Bywaters: Henoch Schönlein Purpura.
INSTITUTE OF NEUROLOGY, National Hospital, Queen Square, W.C.1
5 P.M. Dr. Douglas McAlpine: Multiple Sclerosis.
OXFORD UNIVERSITY
8 P.M. (Radcliffe Infirmary.) Prof. Henry K. Beecher (Harvard): Early Care of Severely Wounded Men.

Tuesday, 9th

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, W.C.2
3.45 P.M. Dr. C. P. Rhoads: Soluble Puzzle of Cancer Control. (Imperial Cancer Research Fund lecture.)
ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1
5.30 P.M. *Experimental Medicine.* Dr. Eric Neil, Dr. B. G. B. Lucas, Mr. D. N. Ross: Hypothermia.
8 P.M. *Psychiatry.* Dr. William Sargant: Aim and Method in Treatment—20 Years of British and American Psychiatry. (Presidential address.)
INSTITUTE OF DERMATOLOGY, Lisle Street, London, W.C.2
5.30 P.M. Dr. R. M. B. MacKenna: The Sebaceous Glandular System.
MANCHESTER MEDICAL SOCIETY
8 P.M. (Clinical Sciences Building, York Place, Manchester, 13.) *Surgery.* Mr. S. M. Milner: Business as Usual. (Presidential address.)

Wednesday, 10th

ROYAL SOCIETY OF MEDICINE
4.30 P.M. *Physical Medicine.* Mr. D. J. Browne, Dr. Trevor Howell: Joint Contractures.
POSTGRADUATE MEDICAL SCHOOL OF LONDON
2 P.M. Dr. F. W. Wolff: Biochemistry of Diabetes.
INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr. E. J. Moynahan: Connective Tissue.
INSTITUTE OF DISEASES OF THE CHEST, Brompton, S.W.3
5 P.M. Dr. N. Lloyd Rusby: Collagen Disorders with Particular Reference to Respiratory Manifestations.
ROYAL SOCIETY OF TROPICAL MEDICINE, 26, Portland Place, London, W.1
7.30 P.M. Dr. H. A. Reid: Sea Snake Research.
MANCHESTER MEDICAL SOCIETY
4.15 P.M. (Medical School, Manchester, 13.) Dr. J. F. Wilkinson: "What's Bred in the Bone . . ." (Presidential address.)

Thursday, 11th

ROYAL SOCIETY OF MEDICINE
5 P.M. *Ophthalmology.* Mr. W. E. S. Bain: The Other Eye in Acute Glaucoma.
5 P.M. *United Services.* Colonel A. P. Trimble, Lieut.-Colonel D. G. Lewis: Leptospirosis in Malaya.
ALFRED ADLER MEDICAL SOCIETY
8 P.M. (11, Chandos Street, W.1.) Dr. James Moore: Aspects of Modern Psychology.
LIVERPOOL MEDICAL INSTITUTION, 114, Mount Pleasant, Liverpool, 3
8 P.M. Prof. Bryan McFarland: Adjustment to Adversity. (Inaugural address.)
ROYAL COLLEGE OF PHYSICIANS OF EDINBURGH, Edinburgh, 2
5 P.M. Prof. W. J. Tulloch: Medicine as an Aspect of General Biology.
ST. ANDREW'S UNIVERSITY, Queen's College, Small's Wynd, Dundee
5 P.M. Sir Neil Hamilton Fairley, F.R.S.: Amœbiasis.

Friday, 12th

ROYAL COLLEGE OF SURGEONS OF ENGLAND
4 P.M. Prof. W. D. Wright: Diagnostic Tests for Colour-vision (Edridge-Green lecture.)
POSTGRADUATE MEDICAL SCHOOL OF LONDON
10 A.M. Prof. C. A. Wells: Conservation of Renal Function.
4 P.M. Dr. L. Guttman: Care of the Paraplegic.
KING'S COLLEGE HOSPITAL MEDICAL SCHOOL, Denmark Hill, S.E.5
4.30 P.M. Mr. Norman Barrett: The Short Œsophagus. (Thomas Percy Legg lecture.)
INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, London, W.C.1
4.30 P.M. Mr. R. D. Owen: Problems in Pharyngeal and Laryngeal Surgery.
INSTITUTE OF NEUROLOGY
5 P.M. Prof. E. Herman (Poland): Tonic Plantar Reflex and its Localising Significance.

The Master's day service of the Society of Apothecaries of London is to be held on Sunday, Oct. 21, at 11.15 A.M. at the Church of St. Mary, Aldermary (opposite Mansion House station).

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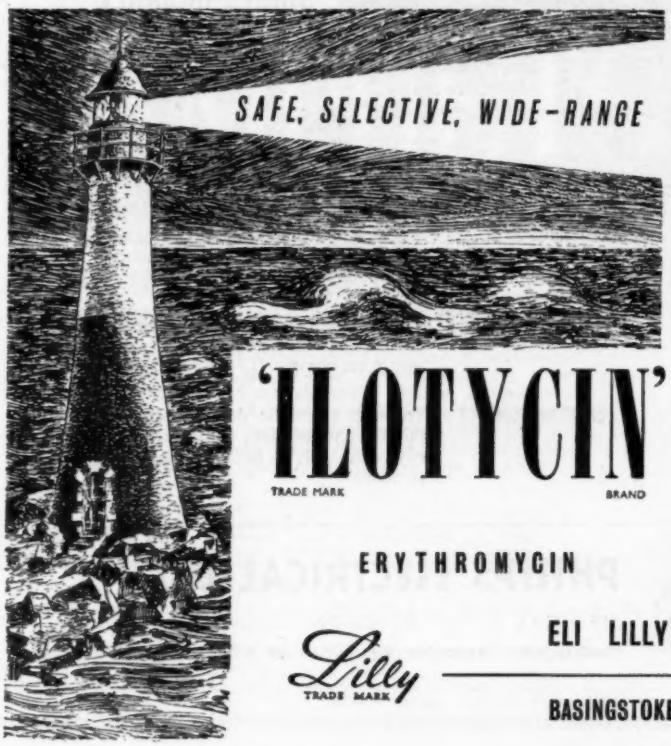

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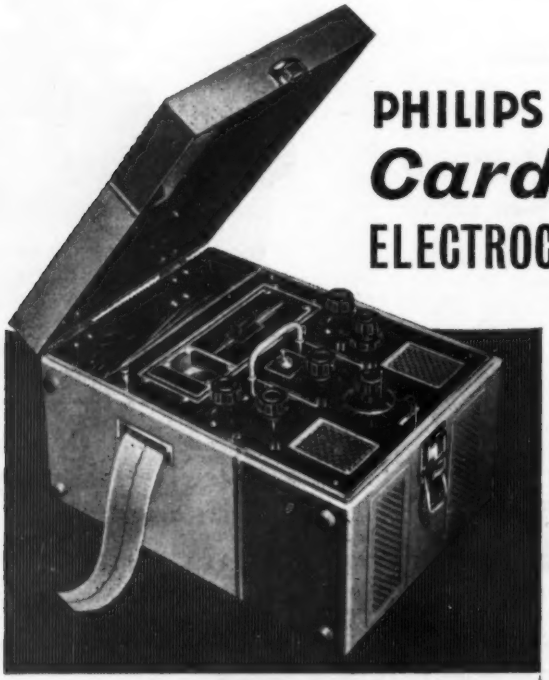

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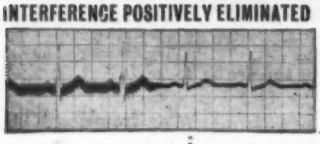

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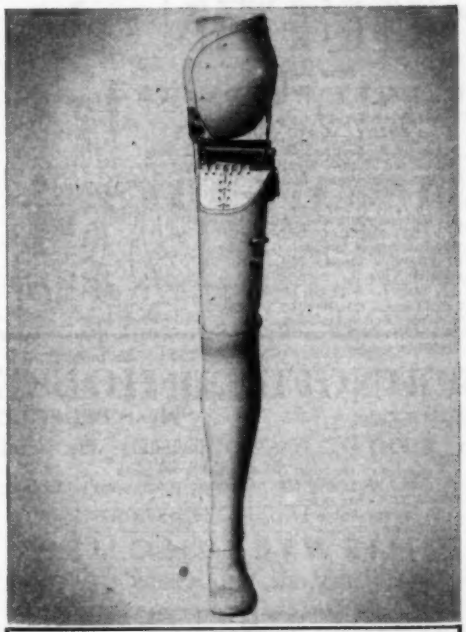

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Academic and Educational

THE UNIVERSITY OF MANCHESTER
DEPARTMENT OF THE EDUCATION OF THE DEAF

COURSE FOR MEDICAL OFFICERS OF HEALTH

A course arranged by the Department of the Education of the Deaf, for a limited number of Medical Officers engaged in the Public Health Service, will be held in the University from 12TH to 15TH FEBRUARY, 1957, inclusive. The course of instruction will include the principles and practice of screening and diagnostic tests of hearing and home-guidance to the parents of deaf children of pre-school and school age. Fee for the course will be 4 guineas.

Applications should be made to the Department of Education of the Deaf, The University, Manchester, 13.

UNIVERSITY OF EDINBURGH

BOOTS RESEARCH FELLOWSHIP IN NURSING

Applications are invited for the Boots Research Fellowship in Nursing, tenable at the Department of Public Health and Social Medicine in the University of Edinburgh. The Fellowship is awarded for research into some aspect of nursing. The initial appointment is for 2 years, but may be renewed. The stipend is £850 p.a. and up to £150 p.a. is available for necessary expenses connected with the prosecution of the research. Candidates must give evidence of knowledge of nursing and should possess a University Degree.

Applications, with the names and addresses of 2 persons for reference, should be sent to the Dean of the Faculty of Medicine by 31st October, 1956.

CHARLES H. STEWART, Secretary to the University.

COLINDALE HOSPITAL, London, N.W.9

A CLINICAL COURSE will be held on 16TH, 17TH, and 18TH OCTOBER. Fee £3 3s. (excluding accommodation).

Further information from the Secretary, Tuberculosis Educational Institute, Tavistock House North, Tavistock-square, London, W.C.1.

THE LONDON HOSPITAL MEDICAL COLLEGE

COURSE IN ADVANCED MEDICINE

A Postgraduate Course in Medicine will be held at The London Hospital commencing MONDAY, 7TH JANUARY, and finishing FRIDAY, 15TH MARCH, 1957. Classes will be held on Mondays, Wednesdays and Fridays. The course will be limited to 24 students.

Applications should be made to the Dean. The fee for the whole course will be 35 guineas, and for Old Londoners 15 guineas.

H. B. MAY, M.A., M.D., F.R.C.P., Dean.

The London Hospital Medical College, Turner-street, E.1.

THE HEBERDEN SOCIETY

On FRIDAY, 19TH OCTOBER, 1956, at 8.30 P.M., Dr. WALTER BAUER, F.A.C.P., will deliver the HEBERDEN ORATION FOR 1955 at The Royal Society of Medicine, London, W.1. He is to speak on "Research and the Rheumatic Diseases."

Members of the medical profession are cordially invited to attend.

THE ROYAL SOCIETY

SCIENTIFIC PUBLICATIONS GRANTS

Applications for grants from the second allotment of the Government Grant for Scientific Publications for the year 1956 should be made as soon as possible. No application can be considered which is received later than 15TH NOVEMBER, 1956. This grant is provided for the assistance of scientific publications in the United Kingdom, particularly but not exclusively those of scientific societies and institutions of a national character. A small part of the grant is available for the assistance of the libraries of scientific societies. Applications are receivable only from societies and institutions in the United Kingdom and individuals of British nationality.

Applications will be considered at the same time for grants from funds made available by the Wellcome Trust for the support of publications dealing with research in the field of medical and allied sciences.

Forms of application may be obtained from the Assistant Secretary, The Royal Society, Burlington House, London, W.1.

MIDDLESEX HOSPITAL, W.1. Applications are invited for the post of ASSISTANT to the Department of Surgical Studies, vacant 1st November, 1956. Commencing salary within the range of £1000–£1300 p.a. according to age and experience.

Applications, stating age, qualifications, &c., and nominating 3 referees, should reach the Secretary of the Medical School by Wednesday, 31st October, 1956.

ST. MARY'S HOSPITAL MEDICAL SCHOOL (University OF LONDON), Paddington, W.2. Applications are invited for the appointment of LECTURER IN MORBID ANATOMY for a period of 3 years from 1st January, 1957. Salary scale £1000–£100–£1300 together with superannuation and children's allowance. Considerable time available for experimental work.

Applications (2 copies), with the names of 3 referees, should be sent by 31st October, 1956, to the Secretary, St. Mary's Hospital Medical School, from whom further particulars may be obtained.

THE LONDON HOSPITAL MEDICAL COLLEGE. Applications are invited for the post of ASSISTANT PATHOLOGIST in the Department of Cancer Research, which is sponsored by the British Empire Cancer Campaign. Initial salary, according to qualifications and experience, on a scale £900–£100–£1300 p.a.

Applications, together with the names of 2 referees, to be forwarded within 14 days to the Secretary, The London Hospital Medical College, Turner-street, London, E.1.

MEDICAL RESEARCH COUNCIL. Assistant (Senior House Officer status) required in Department for Research in Industrial Medicine, London Hospital. Previous experience in industrial medicine not essential.

Apply, stating age, qualifications and experience, to The Director, Dr. DONALD HUNTER.

UNIVERSITY OF BELFAST. The Senate of The Queen's University of Belfast invites applications for a post of LECTURER IN PATHOLOGY with special reference to forensic medicine and PATHOLOGIST to the Ministry of Home Affairs of the Government of Northern Ireland. The post will date from 1st January, 1957, or such later date as may be agreed. The salary scale is £1300–£50–£1950 plus provision for superannuation. In certain circumstances the salary may rise to a maximum of £2050. Initial placing on the salary scale will depend on qualifications and experience.

Applications should be submitted by 30th November, 1956. Further particulars may be obtained from G. R. COWIE, M.A., LL.B., Secretary.

QUEEN'S UNIVERSITY, Kingston, Canada. Applications are invited for the post of LECTURER IN NEUROSURGERY. The appointee will also be Consultant in Neurosurgery at the Kingston General Hospital, and will receive appointments at Mental Hospitals associated with the University and the Department of Health of Ontario. He must take up his appointment within the next 2 years and might be required to undergo further postgraduate training before finally assuming the responsibility of the appointment.

Applications should be sent to the Professor of Surgery, Queen's University, Kingston, Ontario, together with 3 copies each of 6 testimonials and details of the candidate's education and service with the armed forces.

Hospital Services : Senior Appointments

ROYAL MARSDEN HOSPITAL, Fulham-road, S.W.3. Applications are invited for the post of Full-time PATHOLOGIST (Consultant) in charge of the Department of Morbid Anatomy.

Applications (12 copies), quoting age, education, experience, and giving the names of 3 referees, to reach the House Governor, by 29th October, 1956.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for the appointment of a CONSULTANT DERMATOLOGIST for 2 notional half-days a week to the Woolwich Group of hospitals for work primarily at Goldie Leigh Hospital, which caters for dermatological conditions of all kinds in children. Candidates must have had wide experience in dermatology and possession of a higher qualification is desirable. The appointment will be in accordance with the terms and conditions of service of hospital medical and dental staffs (England and Wales). Applicants may visit the Hospital concerned.

Apply, stating nationality, age, sex, qualifications, and experience, including details of present appointment and of war service, together with the names and addresses of 3 referees, to the Secretary, Advisory Appointments Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, London, W.1, not later than 20th October, 1956.

SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD requires Part-time CONSULTANT OPHTHALMOLOGIST (3 half-days per week) in the Lambeth Group of hospitals, for duties at the Royal Eye Hospital, St. George's-circus, S.E.1.

Applications by letter (5 copies), giving date of birth, qualifications, experience, and names of 3 referees, to Secretary (S.I.), South West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, by 3rd November, 1956. Applicants may visit Hospital by local arrangement.

SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD requires Part-time CONSULTANT NEUROLOGIST (5 half-days per week) for duty at general and mental hospitals in the Eastern Area of the Board's Region. The scope of the appointment may be enlarged later but initially the duties will include regular sessions at and/or occasional visits to, the undermentioned hospitals, the average number of hours per week required at each being provisionally assessed as follows :—

Fulham Hospital, S.W.6—3½
Worthing Hospital, Sussex—3½
Farnham Hospital, Surrey—2
Cane Hill (Mental) Hospital, Coulsdon, Surrey—1
Warlingham Park (Mental) Hospital, Surrey—1
Long Grove (Mental) Hospital, Epsom, Surrey } 2
The Manor (M.D.) Hospital, Epsom, Surrey }
Holloway Sanatorium, Virginia Water, Surrey }

It is intended that the Consultant appointed should arrange the frequency of his visits with each of the hospitals concerned.

Applications by letter (5 copies), giving date of birth, qualifications, experience, and names of 3 referees, to Secretary (S.I.), South West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, by 3rd November, 1956. Applicants may visit hospitals by local arrangement.

ST. GEORGE'S HOSPITAL, S.W.1. Applications are invited for a CONSULTANT post in Neurosurgery. The work will be chiefly at the Atkinson Morley Hospital, Wimbledon, in the Neurosurgical Department of St. George's Hospital. Candidates must be Fellows of the Royal College of Surgeons (England). The appointment will be for 7 notional half-days per week, and remuneration and conditions of service will be those applicable to part-time Consultant staff under the National Health Service. The successful candidate will be required to take up duty as soon as possible after 1st January, 1957.

Applications, stating age, education, qualifications and experience, together with the names and addresses of 3 referees, should reach the undersigned not later than 10th November, 1956. P. H. CONSTABLE, House Governor.

ST. PETER'S, ST. PAUL'S AND ST. PHILIP'S HOSPITALS, Henrietta-street, W.C.2. Applications are invited for the post of Whole-time ASSISTANT PATHOLOGIST (Senior Hospital Medical Officer). Good general training and special experience in bacteriology and serology essential. Opportunities for research. Laboratory at St. Paul's may be visited by appointment.

Applications (9 copies), stating age, qualifications and experience, and enclosing the names of 3 referees, to the House Governor by 3rd November, 1956.

BIRMINGHAM REGIONAL HOSPITAL BOARD. Part-time CONSULTANT NEUROLOGIST (7 notional half-days weekly). Duties at North Staffs Royal Infirmary, City General Hospital, Stoke-on-Trent (6 notional half-days), and at the Midland Centre for Neurosurgery, Smethwick (1 notional half-day). Higher qualification and considerable experience specialty essential. Must reside 5 miles radius Stoke-on-Trent.

Applications (15 copies), naming 3 referees, to Secretary, 10, Augustus-road, Birmingham, 15, by 22nd October. Candidates may visit hospitals.

BIRMINGHAM REGIONAL HOSPITAL BOARD. 3 Whole-time ASSISTANT PSYCHIATRISTS. Salary £1575–£2025 p.a.

(*a*) **St. Matthew's Hospital, Burntwood** (1312 Beds). Non-resident.

(*b*) **Shelton Hospital, Shrewsbury** (972 Beds). Resident/non-resident.

(*c*) **Coleshill Hall Hospital, Warwickshire** (1358 Beds—Mental Deficiency). Resident (single accommodation only).

Experienced specialty required.

Applications (15 copies), naming 3 referees, to Secretary, 10, Augustus-road, Birmingham, 15, by 22nd October. Candidates may visit hospitals.

EAST ANGLIAN REGIONAL HOSPITAL BOARD. ASSISTANT RADIOTHERAPIST (whole-time), Ipswich and East Suffolk Hospital. Higher qualification and wide experience in specialty necessary. Salary scale £1575–£2025.

Applications (8 copies), stating age, experience, and names of 3 referees, to the Board's Senior Administrative Medical Officer, 117, Chesterton-road, Cambridge, by 15th October, 1956. Candidates invited to visit Hospital by direct arrangement with Hospital Management Committee Secretary, Ipswich and East Suffolk Hospital (Anglesea Road Wing), Ipswich.

LEEDS REGIONAL HOSPITAL BOARD.

Part-time CONSULTANT in Dentistry (2 sessions per week) for duties mainly at Clayton Hospital, Wakefield, together with additional duties at other hospitals in the Wakefield, Pontefract, Dewsbury, and Goole areas.

Part-time CONSULTANT ANÆSTHETIST (9 sessions per week) for duties in the Halifax area. The person appointed to reside in Halifax.

Applications, stating age, qualifications and details of appointments held showing dates, together with the names and addresses of 3 referees, to the Secretary, Park-parade, Harrogate, not later than 20th October, 1956.

LIVERPOOL REGIONAL HOSPITAL BOARD. Applications are invited for the post of Part-time CONSULTANT ANÆSTHETIST on maximum sessions with duties mainly at hospitals in the St. Helens and Warrington Groups. Candidates must have had at least 5 years recognised training and experience in anæsthesia, and must be Fellows of the Faculty of Anæsthetists, or already hold a Consultant post.

Forms of application from, and to be returned to, Dr. T. Lloyd Hughes, Senior Administrative Medical Officer, Liverpool Regional Hospital Board, 19, James-street, Liverpool, 2, to be received not later than 27th October, 1956.

VINCENT COLLINGE, Secretary to the Board.

AMENDED ADVERTISEMENT

LIVERPOOL REGIONAL HOSPITAL BOARD. Applications are invited for the post of ASSISTANT PÆDIATRIC SURGEON (Consultant) either whole-time or on maximum part-time sessions with duties mainly at Alder Hey Children's Hospital and some duties at Birkenhead Children's Hospital. The successful candidate will work in the pædiatric surgical team under the existing Senior Consultants.

Forms of application from, and to be returned to, Dr. T. Lloyd Hughes, Senior Administrative Medical Officer, Liverpool Regional Hospital Board, 19, James-street, Liverpool, 2, to be received not later than 27th October, 1956.

VINCENT COLLINGE, Secretary to the Board.

NEWCASTLE REGIONAL HOSPITAL BOARD. North WEST DURHAM HOSPITAL MANAGEMENT COMMITTEE. (Population: 140,000.) (Main hospital: Shotley Bridge General, 535 Beds.) SENIOR CASUALTY OFFICER (whole-time). Duration of tenure of post not exceeding 4 years. The Senior Casualty Officer will be required, subject to the supervision of the Senior General Surgeon and Orthopædic Surgeon, to organise the casualty work throughout the Group. To reside near main hospital. Single accommodation available. Salary within range of £1475–£2025 p.a.

Applications, with names and addresses of 3 referees, to Senior Administrative Medical Officer, Benfield-road, Newcastle upon Tyne, 6, within 28 days.

SCOTLAND. NORTH-EASTERN REGIONAL HOSPITAL BOARD. Applications are invited from registered medical practitioners having experience in clinical chemistry for the full-time post of CLINICAL PATHOLOGIST at Woodend General Hospital, Aberdeen. The officer appointed will be on the staff of the Aberdeen General Hospitals. The salary will be on the scale £1575–£50–£2025 p.a. with appropriate scale placing. Terms and conditions of medical and dental staffs as set up by regulations will apply to the post.

Applications (12 copies), together with the names of 2 referees, should be submitted before 22nd October, 1956, to the Secretary, 1, Albyn-place, Aberdeen, from whom further particulars may be obtained.

NORTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Full-time ASSISTANT PSYCHIATRIST (Senior Hospital Medical Officer grade) at Runwell Hospital, near Wickford, Essex. Single accommodation only.

Applications (6 copies), and names of 3 referees, should reach the Secretary, 11A, Portland-place, London, W.1, by Saturday, 20th October.

SCOTLAND. SOUTH-EASTERN REGIONAL HOSPITAL BOARD. Applications are invited for the appointment of DEPUTY PHYSICIAN-SUPERINTENDENT (whole-time Consultant) to the Fife Mental Hospitals.

Applications, giving particulars of age, previous experience, and qualifications, together with the names of 3 referees, should be sent to the Secretary, South-Eastern Regional Hospital Board, Scotland, 11, Drumsheugh-gardens, Edinburgh, 3, by 27th October. Further particulars on application.

SCOTLAND. WESTERN REGIONAL HOSPITAL BOARD. Applications are invited for the appointment of Temporary Whole-time ASSISTANT BACTERIOLOGIST based at Ayrshire Central Hospital, Irvine. The appointment, which will be vacant from 28th October, 1956, will be for a period of 3 years. Salary (at age 32 and over) on the scale £1575–£50–£2025.

Applications (12 copies), stating date of birth, qualifications, experience, present appointment, and the names of 3 referees, to reach the Secretary, Western Regional Hospital Board, 64, West Regent-street, Glasgow, C.2, not later than 15th October, 1956.

SCOTLAND. WESTERN REGIONAL HOSPITAL BOARD. Applications are invited for the following appointments:—

OPHTHALMOLOGIST in charge of beds at Stobhill Hospital, Glasgow, and ASSISTANT OPHTHALMOLOGIST to the Glasgow Eye Infirmary. The appointment is of Consultant grading and will be held on a part-time basis of 8 notional half-days per week.

Whole-time SENIOR CASUALTY OFFICER associated with the Orthopædic Department, Royal Alexandra Infirmary, Paisley. Salary (at age 32 and over) on the scale £1575–£50–£2025.

Whole-time ASSISTANT RADIOLOGIST based at the Dumfries and Galloway Royal Infirmary, Dumfries. Salary (at age 32 and over) on the scale £1575–£50–£2025.

Whole-time ASSISTANT RADIOTHERAPIST based at the Western Infirmary, Glasgow, with duties at other hospitals as may be required by the Regional Radiotherapy Service. Salary (at age 32 and over) on the scale £1575–£50–£2025.

Whole-time ASSISTANT CHEST PHYSICIAN with duties in the Mass Radiography Unit for the City of Glasgow. Salary (at age 32 and over) on the scale £1575–£50–£2025.

These appointments are subject to the National Health Service (Scotland) superannuation regulations.

Applications (16 copies), stating date of birth, qualifications, experience, present appointment, and the names of 3 referees, to reach the Secretary, Western Regional Hospital Board, 64, West Regent-street, Glasgow, C.2, not later than 30 days after the publication of this advertisement.

SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD requires Whole-time ASSISTANT PSYCHIATRIST (Senior Hospital Medical Officer grade) at West Park Hospital, Epsom. Candidates should have D.P.M., wide experience in psychiatry is essential, and good knowledge of general medicine desirable.

Applications by letter (5 copies), giving date of birth, qualifications, experience, and names of 3 referees, to Secretary (S.I.), South West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, by 3rd November, 1956. Applicants may visit Hospital by local arrangement.

SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD requires Whole-time ASSISTANT PSYCHIATRIST (Senior Hospital Medical Officer grade) at Horton Hospital, Epsom. Candidates should possess D.P.M., and have had out-patient experience. Successful candidate will be expected to take active interest in occupational therapy.

Applications by letter (5 copies), giving date of birth, qualifications, experience, and names of 3 referees, to Secretary (S.I.), South West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, by 3rd November, 1956. Applicants may visit Hospital by local arrangement.

SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD requires Whole-time ASSISTANT PSYCHIATRIST (Senior Hospital Medical Officer grade) at St. Ann's Hospital, Canford Cliffs, Bournemouth (68 Beds, for the treatment of psycho-neurotic and early psychotic disorders on a non-legal order basis, and with outpatient facilities). Candidates should possess D.P.M.

Applications by letter (5 copies), giving date of birth, qualifications, experience, and names of 3 referees, to Secretary (S.I.), South West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, by 3rd November, 1956. Applicants may visit Hospital by local arrangement.

WESTERN AUSTRALIA. ROYAL PERTH HOSPITAL. Applications are invited from legally qualified medical practitioners for the full-time post of DIRECTOR OF ANÆSTHESIA. Salary £A3100 p.a. Conditions equivalent to State Public Service, including long service leave and provision for superannuation. The Royal Perth Hospital is the main Teaching Hospital associated with the University of Western Australia. Applicants must possess a Senior Degree in Anæsthesia or its equivalent. Inquiries regarding the Hospital's medical services should be addressed to the Medical Superintendent of this Hospital.

In addition to all relevant personal details, applications must include particulars of qualifications, experience, publications; the names of 2 referees; and should reach the undersigned on or before 31st October, 1956. JOSEPH GRIFFITH, Administrator.

SHEFFIELD. THE UNITED SHEFFIELD HOSPITALS. Applications invited for the post of Whole-time or maximum Part-time (9 notional half-days) CONSULTANT in Anæsthetics. Wide experience and F.F.A.R.C.S. essential.

Applications (16 copies), stating age, qualifications and experience, with the names of 3 referees, should be sent not later than 31st October, 1956, to the Chief Administrative Officer, The United Sheffield Hospitals, West-street, Sheffield, 1, from whom further particulars may be obtained.

Hospital Services : Junior Appointments

BOLINGBROKE HOSPITAL, Wandsworth Common, S.W.11. HOUSE SURGEON (resident), required from 19th October, 1956. Open to registered practitioners and pre-registration candidates.

Apply Hospital Secretary, enclosing copies of 3 recent testimonials, by 8th October, 1956.

CENTRAL MIDDLESEX HOSPITAL, Acton-lane, Park Royal, London, N.W.10. Pre-registration RESIDENT HOUSE OFFICER required in Obstetric and Gynæcological Department. Post approved for D.Obst.R.C.O.G. and M.R.C.O.G. examinations. Pre-registration candidates only will be considered. Appointment for 6 months from 18th November.

Applications, with 2 testimonials, to Medical Director by 13th October.

CONNAUGHT HOSPITAL, Walthamstow, E.17. (118 Beds.) Applications are invited for the post of SECOND CASUALTY OFFICER with duties in the Department of Orthopædic and Traumatic Surgery (Senior House Officer grade). Recognised for F.R.C.S. Salary £745 p.a., less £150 p.a. for board, lodging, &c.

Applications, with full details and copies of 2 recent testimonials, should be sent immediately to Secretary, Hospital Management Committee, Forest Group, Langthorne-road, E.11.

ELIZABETH GARRETT ANDERSON HOSPITAL, Euston-road, N.W.1. ROYAL FREE HOSPITAL GROUP. Applications are invited from pre-registration and registered Women medical practitioners for the post of FIRST HOUSE SURGEON, with charge of general surgical beds. Appointment for 6 months from 1st December, 1956. Salary according to Ministry of Health scale for House Officers.

Applications, with copies of 3 recent testimonials, should be sent to the Secretary, Elizabeth Garrett Anderson Hospital, by 10th October, 1956.

ELIZABETH GARRETT ANDERSON HOSPITAL, Euston-road, N.W.1. ROYAL FREE HOSPITAL GROUP. Applications are invited from pre-registration and registered Women medical practitioners for the post of SECOND HOUSE PHYSICIAN. Appointment for 6 months from 1st December, 1956. Salary according to Ministry of Health scale for House Officers.

Applications, with copies of 3 recent testimonials, should be sent to the Secretary, Elizabeth Garrett Anderson Hospital, by 16th October, 1956.

HACKNEY HOSPITAL, London, E.9. (General—841 Beds.) Applications for the 6-months resident appointment of CASUALTY OFFICER AND E.N.T. HOUSE SURGEON (House Officer grade) should be sent immediately to the Secretary, above address, quoting HH/CHO.

HOSPITAL OF ST. JOHN AND ST. ELIZABETH, 60, Grove End-road, London, N.W.8. Applications are invited from pre-registration or registered medical practitioners (Male) for the appointment of HOUSE SURGEON, to become vacant on Monday, 19th November, 1956. This post is recognised for purposes of the F.R.C.S. (Eng.). Appointment will be for a period of 6 months. National Health Service salary.

Applications should reach the Secretary on or before Friday, 26th October, together with copies of 3 recent testimonials.

ISLINGTON CHEST CLINIC. Registrar required for duties in Chest Clinic and beds at Whittington Hospital, N.19. Previous experience in treatment of tuberculosis essential. Clinic and Hospital may be visited by appointment.

Application forms obtainable from, and returnable to, Group Secretary, 46, Cholmeley-park, N.6, by 15th October, 1956.

LONDON CHEST HOSPITAL. 2 vacancies occur 1st December, 1956, for RESIDENT HOUSE PHYSICIAN. Appointment for 6 months, 4 in London, 2 at the Country Branch, near Letchworth, and post graded as House Officer. Duties include work in the Outpatient Department and Refill Clinic, as well as in wards.

Applications, stating date of birth, qualifications with dates, and previous appointments held, with copies of 3 testimonials, should reach the undersigned not later than 23rd October.

THOMAS BROWN, House Governor.

London Chest Hospital, E.2.

MILE END HOSPITAL, Bancroft-road, London, E.1. (484 Beds.) ANÆSTHETIST (Senior House Officer). Recognised for F.F.A.R.C.S. Post vacant 26th October, 1956.

Application forms, obtainable from Physician-Superintendent, to be returned by 19th October, 1956, with copies of not more than 3 testimonials.

MILE END HOSPITAL, Bancroft-road, London, E.1. (484 Beds.) CASUALTY AND RECEIVING-WARD OFFICER (Senior House Officer). Recognised for F.R.C.S. Post vacant 8th November, 1956.

Application forms, obtainable from Physician-Superintendent, to be returned by 19th October, 1956, with copies of not more than 3 testimonials.

NORTH MIDDLESEX HOSPITAL, Edmonton, N.18. SENIOR HOUSE OFFICER in Surgery, resident, required for 16th November. General surgery, trauma and orthopædics. Post recognised for F.R.C.S.

Applications (in own handwriting), stating age, nationality, qualifications (Primary F.R.C.S. desirable), experience, with copies of recent testimonials or names of 2 referees, to Secretary of Hospital by 16th October.

NORTH MIDDLESEX HOSPITAL, Edmonton, N.18. RESIDENT ANÆSTHETIST (Senior House Officer) required with previous anæsthetic experience. Appointment for 1 year. Hospital is recognised for training for D.A. and F.F.A.R.C.S., and offers a wide experience in anæsthetics (over 10,000 operations a year).

Applications, stating age, nationality, qualifications, experience, with copies of recent testimonials and/or names of 2 referees, to Secretary of Hospital by 16th October.

NORTH MIDDLESEX HOSPITAL, Edmonton, N.18. Applications are invited for the post of CLINICAL ASSISTANT in the Skin Department. 1 weekly session (Wednesday afternoon). Salary £175 p.a.

Applications, stating age, qualifications, experience, nationality with copies of testimonials and/or names of 2 referees, to Secretary of Hospital by 16th October.

NATIONAL HOSPITALS FOR NERVOUS DISEASES. Applications are invited from registered medical practitioners for the appointment of ASSISTANT HOUSE PHYSICIAN (non-resident) at The National Hospital, Queen-square, W.C.1. The post carries the grade of Senior House Officer. The appointment will be for 6 months.

Applications, with names of 3 referees, to be sent to the undersigned not later than 27th October, 1956.

H. EWART MITCHELL,
Secretary to the Board of Governors.

The National Hospital, Queen-square, London, W.C.1.

NATIONAL HOSPITALS FOR NERVOUS DISEASES. Applications are invited from registered medical practitioners for the appointment of HOUSE SURGEON at The National Hospital, Queen-square, W.C.1, commencing 1st December, 1956. This post carries the grade of Registrar.

Applications, giving the names of 3 referees, to be sent to the undersigned not later than 27th October, 1956.

H. EWART MITCHELL,
Secretary to the Board of Governors.

PRINCE OF WALES'S GENERAL HOSPITAL, N.15. (248 Beds.) Applications are invited from qualified medical practitioners for appointment as RESIDENT JUNIOR HOUSE SURGEON for casualty (pre-registration first or second post) for a period of 6 months, vacant 1st December, 1956.

Application form from Secretary, Tottenham Group Hospital Management Committee (Group 4), The Green, N.15, to be returned by 27th October, 1956.

QUEEN CHARLOTTE'S AND CHELSEA HOSPITALS. CHELSEA HOSPITAL FOR WOMEN. HOUSE SURGEON (Senior House Officer), resident post, tenable for 1 year from 1st December, 1956.

Applications to the Secretary to the Board of Governors by 13th October, 1956, on forms obtainable from 339, Goldhawk-road, London, W.6.

QUEEN ELIZABETH HOSPITAL FOR CHILDREN MANAGEMENT COMMITTEE. Hackney-road, E.2, Shadwell, E.1, and BANSTEAD WOOD, SURREY. HOUSE OFFICERS (2). Appointments will be made for 2 consecutive periods of 6 months commencing 1st December, 1956. First period as House Physician and second as House Surgeon and Casualty Officer.

Application forms may be obtained from the Secretary at Hackney-road and should be returned with copies of not more than 3 testimonials on or before 22nd October, 1956.

ROYAL FREE HOSPITAL GROUP. Hampstead General HOSPITAL AND ELIZABETH GARRETT ANDERSON HOSPITAL. Applications are invited for the post of REGISTRAR to the E.N.T. Department at the Hampstead General Hospital and Elizabeth Garrett Anderson Hospital. Applicants should be registered practitioners of not more than 10 years standing.

Application forms may be obtained from the Secretary to the Board of Governors, Royal Free Hospital, Gray's Inn-road, W.C.1, to whom they should be returned not later than 26th October, 1956.

ROYAL NATIONAL ORTHOPÆDIC HOSPITAL, Brockley Hill, STANMORE, MIDDLESEX. Applications are invited for the post of RESIDENT SENIOR HOUSE OFFICER for a period of 6 months : duties to commence 21st December, 1956.

Applications to be received by 31st October. Forms of application can be obtained from the House Governor at 234, Great Portland-street, London, W.1.

ROYAL NORTHERN HOSPITAL, N.7. North West METROPOLITAN REGIONAL HOSPITAL BOARD. REGISTRAR in Radiology, X-ray Diagnostic Department, required at above Hospital. D.M.R.D. essential. Hospital may be visited by direct appointment.

Application forms obtainable from, and returnable to, the Secretary, Royal Northern Hospital, Holloway-road, London, N.7, by 23rd October, 1956.

ST. PETER'S, ST. PAUL'S AND ST. PHILIP'S HOSPITALS. RESIDENT SURGICAL OFFICER (Registrar grade) required for St. Philip's Hospital on 1st December, 1956. Appointment for 6 months with opportunity for extension.

Apply in writing (12 copies), and names of 2 referees, to the House Governor, St. Peter's Hospital, Henrietta-street, W.C.2. Closing date 31st October, 1956.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for an appointment as Whole-time REGISTRAR in Anæsthetics to fill a vacancy in the approved trainee establishment at the Bermondsey and Southwark Group of hospitals, for duties mainly in the Guy's Unit at New Cross General Hospital. The appointment will be in accordance with the terms and conditions of service of hospital medical and dental staffs (England and Wales), and will be for 1 year in the first instance.

Applications, giving particulars of age, qualifications, and experience with relevant dates, together with the names and addresses of 2 referees, to be sent to the Secretary, Registrars Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, W.1, not later than 20th October, 1956.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for an appointment as REGISTRAR in Orthopædic Surgery at the Lewisham Group of hospitals, for duties mainly at Lewisham Hospital, London, S.E.13. The appointment, which may be either resident or non-resident, will be for 1 year in the first instance and is recognised for F.R.C.S. The medical establishment of the Department comprises 2 Registrars and a Senior House Officer under the direction of 2 Consultants; the Casualty Department is separately staffed.

Applications, giving particulars of age, qualifications, and experience with relevant dates, together with the names and addresses of 2 referees, to be sent to the Secretary, Registrars Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, London, W.1, not later than 20th October, 1956.

SOUTH LONDON HOSPITAL FOR WOMEN, Clapham Common, S.W.4. Applications are invited from pre-registration and registered Female medical practitioners for the appointment of OBSTETRIC HOUSE SURGEON. Recognised for the M.R.C.O.G.; appointment is for 6 months from 22nd December, 1956.

Forms of application from the Secretary.

SOUTH LONDON HOSPITAL FOR WOMEN, Clapham Common, S.W.4. Applications are invited from pre-registration and registered Female medical practitioners for the appointment of GYNÆCOLOGICAL HOUSE SURGEON, vacant 20th December, 1956, for 6 months. Recognised for the M.R.C.O.G.

Application forms from the Secretary.

ST. CHARLES' HOSPITAL, Ladbroke-grove, W.10. (581 Beds.) Applications are invited for the post of CASUALTY OFFICER (Senior House Officer), non-resident (1 of 2).

Applications, stating age, qualifications, experience, and names and addresses of 2 referees, to reach Hospital Secretary immediately

ST. MARY ABBOTS HOSPITAL, Marloes-road, Kensington, W.8. Urology. Applications are invited for appointment to the Urology Department of a REGISTRAR (part-time), 5 sessions a week.

Applications (5 copies) to be submitted by 19th October, 1956, on forms obtainable from, and returnable to, Group Secretary (L.133), Fulham and Kensington Hospital Management Committee, 5, Collingham-gardens, London, S.W.5.

ST. MARY'S HOSPITAL, Paddington, W.2. Applications are invited for the post of SENIOR REGISTRAR to the Pædiatric Department at St. Mary's Hospital. Previous experience in pædiatrics is necessary; preference will be given to candidates holding the M.R.C.P. The successful candidate will be required to undertake duties in the Pædiatric Unit at St. Mary's Hospital as well as at the Constituent Children's Hospitals. The appointment will be for a first period of 12 months, with effect from 1st January, 1957, the holder being eligible for reappointment; remuneration to be at Senior Registrar rates. The successful applicant may be eligible to participate in an exchange scheme with the Children's Medical Centre, Boston (Harvard University).

Applications, stating nationality, date of birth, permanent address, qualifications with dates, details and National Health Service gradings of previous and present appointments, together with the names and addresses of 3 referees, should reach ALAN POWDITCH, House Governor, not later than 23rd October, 1956.

ST. MARY'S HOSPITAL, Paddington, W.2. Applications are invited for the post of SENIOR REGISTRAR to the Almroth Wright Ward. The duties of the post require that 6 notional half-days should be devoted to the clinical charge of the 17 beds of the Wright Fleming Institute, together with some laboratory work in connection with cases in the wards. The remaining 5 notional half-days to be devoted to research work in the Wright Fleming Institute of Microbiology. Some previous laboratory experience is desirable. The appointment will be for a period of 12 months as from a date to be arranged. The grading of the post is Senior Registrar and payment will be made by the Board of Governors for 6 notional half-days; payment for the remaining 5 notional half-days will be made by the Wright Fleming Institute. The total salary, therefore, will be equivalent to a whole-time Senior Registrar appointment.

Applications, stating nationality, date of birth, permanent address, qualifications with dates, and details of previous and present appointments, with gradings, together with the names and addresses of 3 referees, should reach ALAN POWDITCH, House Governor, not later than 23rd October, 1956.

ST. MARY'S HOSPITAL, W.2. Applications are invited for the post of SENIOR REGISTRAR to the Department for Diseases of the Skin. Candidates must be registered medical practitioners. Preference will be given to Members of the Royal College of Physicians. The appointment is for a first period of 12 months and the successful candidate, who will be eligible for re-election, will be required to take up his duties as soon as possible.

Applications, stating nationality, date of birth, permanent addresses, qualifications with dates, details and National Health Service gradings of previous and present appointments, together with the names and addresses of 3 referees, should reach ALAN POWDITCH, House Governor, not later than 23rd October, 1956.

ST. MARY'S HOSPITAL, Paddington, W.2. Applications are invited for the post of Whole-time REGISTRAR in the Allergy Clinics (Wright Fleming Institute of Microbiology). Preference will be given to candidates with previous experience in this specialty. The appointment is for a first period of 12 months as from 1st December, 1956; remuneration to be at Registrar rates.

Applications, stating nationality, date of birth, permanent address, qualifications with dates; details and National Health Service gradings of previous and present appointments, together with the names and addresses of 3 referees, should reach ALAN POWDITCH, House Governor, not later than 16th October, 1956.

ST. NICHOLAS HOSPITAL, Plumstead, S.E.18. Senior HOUSE OFFICER (Orthopædic, Fracture and Casualty Departments), vacant early November. Recognised for F.R.C.S. 6 months appointment and may then be renewed. Salary £745 p.a., less £150 p.a. for residence.

Apply to Group Secretary, Memorial Hospital, Woolwich, S.E.18.

ST. NICHOLAS HOSPITAL, Plumstead, S.E.18. Senior HOUSE OFFICER (anæsthetics), vacant early November. Recognised for F.F.A.R.C.S. and D.A. 6 months appointment and may then be renewed. Salary £745 p.a., less £150 p.a. for residence.

Apply to Group Secretary, Memorial Hospital, Woolwich, S.E.18.

ST. ANN'S GENERAL HOSPITAL, N.15. Applications are invited from registered medical practitioners for the appointment of RESIDENT HOUSE SURGEON (Senior House Officer) to above Hospital for a period of 6 months from 17th November, 1956.

Application form from Secretary, Tottenham Group Hospital Management Committee, The Green, N.15, to be returned by 20th October, 1956.

ST. ANN'S GENERAL HOSPITAL, N.15. Applications are invited from registered medical practitioners for the appointment of RESIDENT HOUSE SURGEON (third post) to above Hospital for a period of 6 months from 18th November, 1956.

Application form from Secretary, Tottenham Group Hospital Management Committee, The Green, N.15, to be returned by 20th October, 1956.

THE HOSPITAL FOR SICK CHILDREN, Great Ormond-street, London, W.C.1. There will be vacancies for the following Senior House Officers on 15th January, 1957.

2 HOUSE PHYSICIANS.
2 HOUSE SURGEONS.

Further particulars and form of application, which must be returned not later than Monday, 5th November, 1956, are obtainable from the undersigned.

H. F. RUTHERFORD, House Governor and Secretary.

UNIVERSITY COLLEGE HOSPITAL, Gower-street, London, W.C.1. Applications are invited for the post of REGISTRAR in the Department of Psychological Medicine for 1 year in the first instance from 1st November, 1956, or as soon as possible thereafter.

Applications, with names of 2 referees, to Administrator and Secretary by 17th October, 1956.

UNIVERSITY COLLEGE HOSPITAL, Gower-street, London, W.C.1. Applications are invited for the post of MEDICAL REGISTRAR for 1 year in the first instance from 1st November, 1956, or as soon as possible thereafter. This post will include a period of duty at the Whittington Hospital, London, N.19. Preference will be given to candidates holding higher qualifications.

Applications, with names of 2 referees, to Administrator and Secretary by 17th October, 1956.

WESTMINSTER HOSPITAL, St. John's Gardens, S.W.1. Applications invited for post of RESIDENT CASUALTY OFFICER (Senior House Officer grade) with duties as House Physician in Skin and V.D. Departments for 1 year. Board and lodging £150 p.a.

Applications (11 copies), with names of 2 referees, to House Governor by 17th October.

WOOLWICH GROUP HOSPITAL MANAGEMENT COMMITTEE. CLINICAL ASSISTANT (rheumatic diseases). The appointment is for 1 session per week at Brook General Hospital, Shooters Hill-road, S.E.18, and will be for 1 year in the first instance. Remuneration £175 p.a.

Apply to Group Secretary, Memorial Hospital, Woolwich, S.E.18, by 26th October.

ABERDEEN GENERAL HOSPITALS BOARD OF MANAGEMENT. Applications are invited for the appointment of a JUNIOR HOSPITAL MEDICAL OFFICER in General Medicine at the Aberdeen Royal Infirmary and Woodend General Hospital. Conditions of service in accordance with the terms issued by the Department of Health for Scotland.

Applications, with the names of 2 referees, should be lodged with the Secretary, Aberdeen General Hospitals, P.O. Box No. 92, 62, Queen's-road, Aberdeen, within 14 days of the appearance of this advertisement.

ABERDEEN GENERAL HOSPITALS BOARD OF MANAGEMENT. Applications are invited for the appointment as REGISTRAR in Surgery with main duties in the Aberdeen Royal Infirmary to commence in January, 1957. The post is a whole-time one and is non-resident. Salary and conditions of service in accordance with the terms issued by the Department of Health for Scotland.

Applications, giving details of qualifications and experience, with the names of 2 referees, should be lodged with the Group Secretary, P.O. Box 92, 62, Queen's-road, Aberdeen, within 14 days of the appearance of this advertisement.

ASHFORD HOSPITAL, Ashford, Middlesex. (560 Beds.) STAINES GROUP HOSPITAL MANAGEMENT COMMITTEE. Required, RESIDENT HOUSE OFFICER (Male) for Special Departments (E.N.T., pædi tric, dermatology, &c.). 6 months appointment, vacant 15th October, 1956. Not suitable for pre-registration candidates; offers good experience before general practice.

Applications, stating age, qualifications and experience, with copies of up to 3 recent testimonials, to Medical Director of Hospital.

ASHTON, HYDE AND GLOSSOP HOSPITAL MANAGEMENT COMMITTEE. HOUSE SURGEON required at Ashton-under-Lyne General Hospital. Preference will be given to pre-registration applicants. Recognised for F.R.C.S. (Eng.). Vacant 1st November, 1956.

Applications, with copies of 2 testimonials, to Group Secretary, General Hospital, Ashton-under-Lyne, Lancashire.

BARROW AND FURNESS HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the resident or non-resident post of REGISTRAR in Anæsthetics in the Barrow and Furness Group of hospitals, based at the North Lonsdale Hospital, Barrow-in-Furness. Hospital approved for D.A.

Applications, giving age, details of experience, and names of 3 referees, to Group Secretary, 105, Abbey-road, Barrow-in-Furness.

BANGOR. ST. DAVID'S HOSPITAL. (Specialist Hospital for Women and Children.) Applications are invited for the post of RESIDENT PÆDIATRIC OFFICER (Senior House Officer grade). Preference will be given to candidates with previous experience in neonatal and premature infant care. The Pædiatric Unit is recognised for the D.C.H. Salary according to scale.

Applications, stating age, qualifications and experience, together with the names and addresses of 2 referees, should be forwarded within 10 days of the appearance of this advertisement to the Group Secretary, Caernarvon and Anglesey Hospital Management Committee, Plas Gwyn, Ffriddoedd-road, Bangor, North Wales.

BEDFORD GENERAL HOSPITAL. (439 Beds.) House SURGEON required (mainly orthopædic). Pre- or post-registration: recognised for F.R.C.S. Vacant mid-October. Post offers exceptional opportunities for general experience in busy acute surgical units.

Inquiries and applications, with copies of 2 recent testimonials, to Group Secretary, 3, Kimbolton-road, Bedford.

BEDFORD GENERAL HOSPITAL. (439 Beds.) Resident HOUSE SURGEON (gynæcology and obstetrics) required mid-November. Pre-registration post and recognised for D.Obst. R.C.O.G. The unit comprises 26 gynæcological and 60 obstetric beds and a busy Outpatient Department.

Applications, stating age, experience, qualifications, copies of 2 recent testimonials, to Group Secretary, Bedford Group Hospital Management Committee, 3, Kimbolton-road, Bedford, by 17th October, 1956.

BEDFORD GENERAL HOSPITAL. (439 Beds.) North WEST METROPOLITAN REGIONAL HOSPITAL BOARD. GENERAL SURGICAL REGISTRAR (resident) required at above Hospital which may be visited by direct appointment. Post vacant October.

Application forms obtainable from, and returnable to, Group Secretary, Bedford Group Hospital Management Committee, 3, Kimbolton-road, Bedford, as soon as possible.

BEDFORD (near). BROMHAM HOSPITAL. (434 Beds for mental defectives and 60 at Annexe near Sandy.) REGISTRAR in Psychiatry required (resident). Hospital may be visited by direct appointment with the Medical Superintendent (phone: Oakley 295).

Application forms obtainable from, and returnable to, Secretary, Bedford Group Hospital Management Committee, 3, Kimbolton-road, Bedford

BEVERLEY, YORKSHIRE. WESTWOOD HOSPITAL. (229 Beds.) HOUSE PHYSICIAN (House Officer or Senior House Officer grading according to experience), vacant now. Pre-registration post but fully qualified practitioners may apply.

Applications to Group Secretary.

BOURNEMOUTH. ROYAL VICTORIA HOSPITAL, Shelley-road. BOURNEMOUTH AND EAST DORSET HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of GENERAL HOUSE SURGEON, vacant 5th November, 1956. The appointment is recognised for the F.R.C.S. examination and for pre-registration purposes.

Applications to the Hospital Secretary.

BOURNEMOUTH. ROYAL VICTORIA HOSPITAL. (494 Beds.) BOURNEMOUTH AND EAST DORSET HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of SENIOR HOUSE OFFICER (resident) orthopædic and casualty combined. The post, which becomes vacant on 10th November, is recognised for the F.R.C.S. examination.

Applications to the Hospital Secretary.

BOURNEMOUTH. ROYAL VICTORIA HOSPITAL, Shelley-road. BOURNEMOUTH AND EAST DORSET HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of RESIDENT SENIOR HOUSE OFFICER (anæsthetics). The post, which becomes vacant on 10th November, is recognised for the D.A. and F.F.A.R.C.S., and is tenable for 12 months. Experience with Thoracic Unit available.

Applications to the Hospital Secretary.

BRISTOL (near). HAM GREEN HOSPITAL, Pill, near BRISTOL. Applications are invited for the post of RESIDENT ASSISTANT PHYSICIAN in the Infectious Disease Department (350 Beds) of this Hospital. The Hospital contains a major Poliomyelitis Unit, a Tuberculous Meningitis Treatment Centre, and offers wide experience in acute medicine. Salary and conditions on Junior Hospital Medical Officer scale.

Applications, stating age, qualifications, &c., to the Group Secretary, Ham Green Hospital, Pill, Bristol.

BRISTOL (near). HAM GREEN HOSPITAL, Pill, near BRISTOL. Applications are invited for the post of SENIOR HOUSE OFFICER in the tuberculosis wards (188 Beds) of the above Hospital. The Hospital is fully equipped for the modern treatment of pulmonary tuberculosis including regular major thoracic surgery.

Applications to Secretary, Ham Green Hospital, Pill, near Bristol.

BRIGHTON. ROYAL SUSSEX COUNTY HOSPITAL. (312 Beds.)

2 HOUSE SURGEONS required mid- and end-October.

2 HOUSE PHYSICIANS required mid-October and mid-November.

All posts recognised for pre-registration and F.R.C.S.

Applications, stating usual particulars, and naming 2 referees, to the Administrative Officer, Royal Sussex County Hospital, Brighton, 7.

BRIGHTON. ROYAL ALEXANDRA HOSPITAL FOR SICK CHILDREN, Dyke-road, BRIGHTON. (130 Beds.) Vacancies for HOUSE PHYSICIAN and HOUSE SURGEON for 6 months from 9th and 12th November, 1956, respectively. Both posts offer wide experience in pædiatrics and are recognised for D.C.H.; that of House Surgeon is open to pre-registration candidates.

Applications, stating age, nationality, qualifications, and experience together with copies of recent testimonials, to be sent to the Administrative Officer as soon as possible.

BIRMINGHAM ACCIDENT HOSPITAL, Bath-row, BIRMINGHAM, 15. (215 Beds and 8 House Surgeons.) HOUSE SURGEON (resident) vacant now. Recognised for purpose of Casualty by R.C.S. (Eng.). Teaching programme by Consultant Staff. Appointment for 6 months, some of which may be spent, at applicant's request, in 42-Bedded Medical Research Council's Burns Unit.

Apply, naming 2 referees, to Administrator.

BIRMINGHAM REGIONAL HOSPITAL BOARD. Whole-time SENIOR REGISTRARS in Psychiatry.

(*a*) **All Saints Hospital, Birmingham** (1385 Beds) **and Early Treatment Centre, Ufficulme.** Candidates should be actively interested in research. D.P.M. essential. Higher medical qualifications an advantage.

(*b*) **Shelton Hospital, Shrewsbury** (972 Beds). Wide experience specialty and higher qualification required. Resident.

Application forms from Secretary, Regional Hospital Board, 10, Augustus-road, Birmingham, 15, to be returned by 22nd October. Candidates may visit hospitals.

BIRMINGHAM REGIONAL HOSPITAL BOARD.

(1) **Birmingham (Dudley Road) Group, Dudley Road, Birmingham, 18**

REGISTRAR (anæsthetics) required (780 Beds). Recognised for D.A. and F.F.A.R.C.S. Duties at other hospitals in the Group.

(2) **Coventry and South Warwickshire Groups, 50, Holly-walk, Leamington Spa**

REGISTRAR (psychiatry) for Coventry and South Warwickshire Groups. 7 outpatient sessions at child guidance clinics at Coventry and Nuneaton; Adult clinics at Coventry and Rugby Hospitals. 4 sessions at Central Mental Hospital, near Warwick, which has Neurosis Unit, Psychological Department, Electro-encephalography Department, occupational therapy and all modern treatments. Adequate training for D.P.M. House only available at Central Hospital.

(3) **Stoke-on-Trent Group, Princes-road, Stoke-on-Trent**

REGISTRAR (chest diseases) for Cheshire Joint Sanatorium (305 Beds). Experience general medicine required.

(4) **West Bromwich Group, Edward-street, West Bromwich**

REGISTRAR (general surgery) (144 Beds). Recognised for F.R.C.S. Resident. Married quarters available. Higher qualification an advantage.

Application forms from Group Secretaries, to be returned by 15th October, 1956.

BIRMINGHAM REGIONAL HOSPITAL BOARD. Senior REGISTRAR in Pathology based on Dudley Road Group of hospitals. At least 1 year shall be served in the University Medical School, Teaching Hospitals and/or the Blood Transfusion Service according to the preference of the successful candidate.

Application forms from Secretary, 10, Augustus-road, Birmingham, 15, to be returned by 22nd October, and candidates, may visit Hospitals.

BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS. THE CHILDREN'S HOSPITAL, Ladywood-road, BIRMINGHAM, 16. Applications are invited for the appointment of RESIDENT SENIOR HOUSE OFFICER to work in the Clinical Pathological Department, vacant middle of October, 1956, for 1 year. Applicants should have held resident appointments in a children's hospital or a children's department of a general hospital.

Forms of application may be obtained from the House Governor and should be returned immediately.

G. A. PHALP, Secretary to the Board of Governors.

BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS. Applications are invited for the appointment of SENIOR E.N.T. REGISTRAR (non-resident), Senior Registrar grade, for duties within the United Hospitals. Higher qualification in the specialty necessary. The appointment will be for 1 year in the first instance and subject to annual review. The successful candidate may subsequently be required to spend not more than 2 years in a selected hospital of the Birmingham Regional Hospital Board in accordance with an arrangement for the interchange of Registrars agreed between the 2 Boards.

Forms of application may be obtained from the Secretary, United Birmingham Hospitals, Queen Elizabeth Hospital, Birmingham, 15, and should be returned not later than 13th October, 1956.

BOLTON AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE.

The Royal Infirmary, Bolton (237 Beds)

RESIDENT SENIOR HOUSE OFFICER in Orthopædic Surgery, vacant 29th October, tenable for 12 months and recognised for F.R.C.S.

RESIDENT HOUSE SURGEON for general surgical duties, vacant 18th October, tenable for 6 months and recognised under Pre-registration Service Scheme. Also recognised for F.R.C.S.

Bolton District General Hospital (604 Beds)

RESIDENT HOUSE PHYSICIAN, vacant 9th November, tenable for 6 months and recognised under Pre-registration Service Scheme.

RESIDENT HOUSE SURGEON, vacant 9th November, tenable for 6 months and recognised under Pre-registration Service Scheme. Also recognised for F.R.C.S.

Applications, stating age, nationality, qualifications, experience, and names of 2 referees, to Group Secretary, The Royal Infirmary, Bolton.

CAMBRIDGE. ADDENBROOKE'S HOSPITAL. OBSTETRIC AND GYNÆCOLOGICAL REGISTRAR (non-resident), vacant November for 1 year in the first instance, renewable for second year. The post includes duties at Addenbrooke's and the Maternity Hospitals.

Apply, with full particulars and names of 3 referees, to Secretary by 20th October.

CANTERBURY. NUNNERY FIELDS HOSPITAL. (Chronic sick—136 Beds.) Locum Tenens JUNIOR HOSPITAL MEDICAL OFFICER required for about 4 months, for full-time service at above Hospital.

Further details concerning this appointment will be forwarded on application to Group Secretary, Nunnery Fields Hospital, Canterbury.

CARDIFF. ST. DAVID'S HOSPITAL. Senior House OFFICER urgently required at Accident Unit at above Hospital.

Form of application from Group Secretary, Cardiff Hospital Management Committee, 44, Cathedral-road, Cardiff.

CARDIFF. ST. DAVID'S HOSPITAL. Senior House OFFICER (non-resident) required in Casualty Department of above Hospital on 15th October, 1956.

Form of application from Group Secretary, Cardiff Hospital Management Committee, 44, Cathedral-road, Cardiff.

CARSHALTON. QUEEN MARY'S HOSPITAL FOR CHILDREN. (853 Beds.) ORTHOPÆDIC REGISTRAR, with some surgical duties, required. Applicants are invited to visit the Hospital by appointment with the Physician-Superintendent.

Applications, which should be made on forms obtainable from the Group Secretary, should be returned immediately.

CLACTON AND DISTRICT HOSPITAL, Clacton-on-Sea. (58 Beds.) Applications invited for post of SENIOR HOUSE OFFICER (Resident Surgical Officer). Post tenable for 1 year.

Applications with copies of 3 testimonials, to Group Secretary, Colchester Hospital Management Committee, 14, Pope's-lane, Colchester, Essex.

COLCHESTER HOSPITAL MANAGEMENT COM-MITTEE. Applications are invited for :—

Essex County Hospital, Colchester (188 Beds)

SENIOR HOUSE OFFICER (casualty and radiotherapy). Post recognised for F.R.C.S. ; tenable for 6 months or 1 year.

SENIOR HOUSE OFFICER (anæsthetics). The successful candidate will be called upon to give anæsthetics in other hospitals in the Group. Post recognised for F.F.A.R.C.S. and D.A. ; tenable for 1 year.

Applications, with copies of 3 testimonials, to Group Secretary, 14, Pope's-lane, Colchester, Essex.

COLCHESTER. SEVERALLS HOSPITAL. Junior HOSPITAL MEDICAL OFFICER required (resident or non-resident). Commencing salary £775 p.a., rising to £1075 p.a. Furnished accommodation available for a single officer. There will be scope for work in the use of modern psychiatric methods in the wards.

Applications, with names of 2 referees, should be forwarded to the Medical Superintendent.

COVENTRY AND WARWICKSHIRE HOSPITAL. Senior HOUSE OFFICER (fracture and orthopædics), resident, vacant 30th October. Recognised F.R.C.S.

Applications to Secretary, Group 20 Hospital Management Committee, Stoney Stanton-road, Coventry.

COVENTRY AND WARWICKSHIRE HOSPITAL. (354 Beds.) HOUSE SURGEON (general surgery with some orthopædic duties), pre-registration, resident. Vacant 31st October, 1956.

Apply to Hospital Secretary.

CROYDON GENERAL HOSPITAL. House Surgeon (pre-registration) required as from 10th November, 1956. Post recognised for F.R.C.S.

Application forms obtainable from GEORGE A. PAINES, Group Secretary, Hospital Management Committee, General Hospital, London-road, Croydon, to be returned immediately.

CROYDON GENERAL HOSPITAL. (200 Beds.) Senior CASUALTY OFFICER (Registrar status). Post vacant. Busy Department. Post recognised for Final F.R.C.S. examination. Accommodation may be inspected on application to Hospital Secretary.

Application forms obtainable from GEORGE A. PAINES, Group Secretary, Hospital Management Committee, General Hospital, London-road, Croydon.

CROYDON. MAYDAY HOSPITAL. (611 Beds.) Surgical REGISTRAR (whole-time) resident when on duty. Post vacant early in November. Candidates should have good medical and surgical background and preferably in possession of higher surgical qualification. There are 2 surgical teams at Hospital. Post recognised for Final F.R.C.S. examination.

Application forms obtainable from GEORGE A. PAINES, Group Secretary, Croydon Hospital Management Committee, General Hospital, Croydon.

CHERTSEY, SURREY. ST. PETER'S HOSPITAL (late Botleys Park War Hospital). (430 Beds.) ORTHOPÆDIC HOUSE SURGEON required from 3rd November, 1956. 100 orthopædic beds. Senior House Officer or House Officer (intern grade). Post recognised for F.R.C.S. and Pre-registration Service. Preference given to provisionally registered candidates. Salary in accordance with terms and conditions of National Health Service.

Applications, together with names and addresses of referees, to be sent to the Physician-Superintendent, St. Peter's Hospital, Chertsey, as soon as possible.

CHESTER ROYAL INFIRMARY. Applications are invited for the post of RESIDENT CASUALTY OFFICER (Junior Hospital Medical Officer). The post is recognised for the F.R.C.S.

Applications, giving full details, together with the names and addresses of 2 referees, should be forwarded to the Group Secretary, Chester and District Hospital Management Committee, 5, King's-buildings, Chester.

CHELTENHAM. ST. PAUL'S HOSPITAL. (42 surgical and 93 geriatric beds.) SENIOR HOUSE OFFICER required. Main duties concerned with surgical beds. Person appointed would also be expected to carry out certain duties concerned with geriatric patients.

Applications, giving details of qualifications, experience, and names of 3 referees, to the Group Secretary, General Hospital, Sandford-road, Cheltenham.

CHESTERFIELD ROYAL HOSPITAL. Senior House OFFICER required immediately at above Hospital for Accident and Orthopædic Department. Post recognised for F.R.C.S. training and offers valuable experience. National salary and conditions.

Apply M. H. BOONE, Secretary, Chesterfield Hospital Management Committee.

CHICHESTER GROUP HOSPITAL MANAGEMENT COMMITTEE. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. RADIOLOGY REGISTRAR. Applications are invited for this appointment in Registrar grade (National Health Service conditions, &c.), £850 p.a. first year and £965 second year. Duties at Royal West Sussex, St. Richard's and Graylingwell (Mental) Hospitals, Chichester, and Bognor War Memorial Hospital (General Practitioners have direct reference to 2 of these). The hospitals may be visited by appointment with the Consultant Radiologist.

Forms of application from Group Secretary, 174, Broyle-road, Chichester, Sussex, to be returned by 29th October. Canvassing disqualifies.

CHICHESTER. ROYAL WEST SUSSEX HOSPITAL. (202 acute beds.) RESIDENT HOUSE SURGEON required for 6 months appointment. National salary scale for first, second or third posts. Post approved for pre-registration practitioners. Also recognised for F.R.C.S. 7 residents including Resident Surgical Officer and 3 House Surgeons. Vacant 29th October, 1956.

Applications, stating age, experience, qualifications, with references or names of referees, to Senior Administrative Officer.

DONCASTER HOSPITAL MANAGEMENT COM-MITTEE. HAMILTON ANNEXE, WESTERN HOSPITAL. (Recognised under the regulations for the D.Obst.R.C.O.G. and M.R.C.O.G. (obstetrical experience) and approved for Pre-registration Service under the Medical Act, 1950.) Applications are invited for the post of OBSTETRICAL HOUSE OFFICER (Senior House Officer or pre-registration post), vacant early November.

Applications should be forwarded to the Group Secretary at Doncaster Royal Infirmary by 22nd October.

DONCASTER HOSPITAL MANAGEMENT COM-MITTEE. HOUSE PHYSICIAN (Senior House Officer) required between Western Hospital, Doncaster, and Doncaster Royal Infirmary. Resident at Western Hospital. Post vacant towards end of October.

Applications to the Group Secretary at Doncaster Royal Infirmary.

DONCASTER ROYAL INFIRMARY. (330 Beds.) Applica-tions are invited for the post of RESIDENT ANÆSTHETIST in the grade of Senior House Officer. Post recognised under the regulations for the D.A. Duties to commence beginning of October.

Applications to the Group Secretary, Doncaster Hospital Management Committee, at Doncaster Royal Infirmary.

DOUGLAS, ISLE OF MAN. NOBLE'S ISLE OF MAN HOSPITAL. (160 Beds.) Applications are invited from registered medical practitioners with previous hospital experience, preferably at a teaching hospital, for the post of SENIOR HOUSE SURGEON at this busy General Hospital. The Senior of 4 House Officer posts. The post becomes vacant mid-November, and is suitable for candidate seeking further clinical experience and opportunity for reading for higher qualification. Recognised for F.R.C.S. Salary £745 p.a. with a deduction of £125 p.a. for board, lodging, &c., if resident.

Applications, giving relevant particulars, and copies of 2 recent testimonials, or names and addresses of 2 referees, should be forwarded to the Secretary, Noble's Isle of Man Hospital, Douglas.

DRIFFIELD, YORKSHIRE. EAST RIDING GENERAL HOSPITAL. (247 Beds.) HOUSE PHYSICIAN (first, second or third post), vacant soon. Approved pre-registration post. Fully qualified practitioners may apply. Duties to include acute and chronic sick and casualties. Good general experience for first house appointment.

Apply Group Secretary, Westwood Hospital, Beverley, Yorkshire.

DRIFFIELD, YORKSHIRE. NORTHFIELD SANATOR-IUM. (78 Beds.) SENIOR HOUSE PHYSICIAN, vacant now. Offers experience all branches of tuberculosis within Group, including surgery, M.M.R., and clinics. Time for study. Ex-patients welcome. £150 for full residence.

Applications to Group Secretary, Westwood Hospital, Beverley, Yorkshire.

DUDLEY, STOURBRIDGE AND DISTRICT HOSPITAL GROUP, BIRMINGHAM REGION.

The Guest Hospital, Dudley (154 Beds)

SENIOR HOUSE OFFICER (casualty). Post now vacant.
SENIOR HOUSE OFFICER (anæsthetics). Post now vacant.
SENIOR HOUSE OFFICER (surgical). Post now vacant.

Wordsley Hospital, near Stourbridge (478 Beds)

SENIOR HOUSE OFFICER (surgical). Post vacant October, 1956.

Apply, Group Secretary, Guest Hospital, Dudley.

EXETER. ROYAL DEVON AND EXETER HOSPITAL. Applications are invited from registered medical practitioners for the appointment of SENIOR HOUSE OFFICER (E.N.T. Department—31 Beds), vacant 1st December, 1956. The post is recognised for the F.R.C.S. examination.

Applications, with copies of 2 recent testimonials, to the Hospital Secretary by 20th October, 1956.

EDGWARE GENERAL HOSPITAL, Edgware, Middlesex. (715 Beds.) JUNIOR HOSPITAL MEDICAL OFFICER (non-resident), required in the Casualty Department at above Hospital.

Apply, stating age, nationality, qualifications and experience, together with names and addresses of 2 referees, to Group Secretary, Edgware General Hospital, by 20th October, 1956.

EDGWARE GENERAL HOSPITAL. (715 Beds.) North WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Whole-time NON-RESIDENT SURGICAL REGISTRAR required for general and genito-urinary duties at above Hospital. Post vacant 29th November, 1956. Hospital may be visited by direct appointment with Medical Director.

Application forms obtainable from, and returnable to, Group Secretary, Hendon Group Hospital Management Committee, Edgware General Hospital, Edgware, Middlesex, by 16th October, 1956.

EAST ANGLIAN REGIONAL HOSPITAL BOARD. SURGICAL REGISTRAR, West Norfolk and King's Lynn General Hospital (146 Beds). Recognised for F.R.C.S. Appointment for 1 year, renewable for second year.

Applications, stating age, experience and the names of 3 referees, to Board's Senior Administrative Medical Officer, 117, Chesterton-road, Cambridge, by 15th October, 1956. Candidates invited to visit Hospital by direct arrangement with Hospital Management Committee Secretary at Hospital.

EAST ANGLIAN REGIONAL HOSPITAL BOARD. RADIOLOGICAL REGISTRAR, Norfolk and Norwich Hospital (440 Beds). The department is the centre for consultant radiological services to a large Hospital Group in Norwich, Great Yarmouth and Norfolk. Appointment for 1 year, renewable for second year.

Applications, stating age, experience, and the names of 3 referees, to Board's Senior Administrative Medical Officer, 117, Chesterton-road, Cambridge, by 15th October, 1956. Candidates are invited to visit Hospital by direct arrangement with Hospital Management Committee Secretary at Hospital.

FARNBOROUGH HOSPITAL, Kent. (800 Beds.) Ortho-PÆDIC SENIOR HOUSE OFFICER required immediately for 1 year. Recognised for F.R.C.S. Deduction for residence £150.

Apply, stating age, qualifications with dates, and experience, and naming 3 referees, to Administrative Officer.

GLASGOW, N.1. STOBHILL GENERAL HOSPITAL. Applications are invited for the post of JUNIOR HOSPITAL MEDICAL OFFICER (Male or Female), in the Psychiatric Unit which consists of 180 Beds with 1600 admissions yearly and deals with acute treatable cases; it is recognised for the D.P.M. The appointment will be for 2 years in the first instance.

Applications, stating age, qualifications, and experience, and naming 2 referees, should be sent to the Medical Superintendent.

GLOUCESTER. HORTON ROAD AND CONEY HILL HOSPITALS. (1450 Beds.) Applications invited for the appointment of a JUNIOR HOSPITAL MEDICAL OFFICER. Hospital serves the North Gloucestershire Clinical Area including Gloucester, Cheltenham, Stroud and Forest of Dean. High admission-rate (800). All modern methods of treatment. New units provided for treatment of neurosis and alcoholism. Expanding outpatient services, long-stay annexes, and social clubs. Encouragement and opportunity for study. Salary and conditions Whitley Council. Single accommodation available. Married accommodation a possibility.

Applications, with names of 3 referees, to Physician-Superintendent within 14 days.

HASLEMERE AND DISTRICT HOSPITAL. Guildford GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of Locum RESIDENT SENIOR HOUSE OFFICER (with possibility of 12 months appointment). Post vacant 6th November, 1956. Mainly surgical but with charge of 12 medical beds. Busy General Hospital with easy access to London. Good experience in general and emergency surgery, orthopædic, E.N.T., gynæcological, children, and casualty work. Excellent post for those wishing to enter general practice.

Applications to Hospital Secretary, Haslemere and District Hospital, Haslemere, Surrey.

HEREFORD GENERAL HOSPITAL. (154 Beds.) House OFFICER (general surgery) required, pre-registration post, Hospital recognised by R.C.S. Duties include care of general surgical beds and in addition for 3 months of orthopædic beds and for 3 months of E.N.T. beds.

Applications, with copies of testimonials, to be sent to the Group Secretary, Victoria House, Eign-street, Hereford.

HITCHIN. LISTER HOSPITAL. (317 Beds.) North WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Whole-time MEDICAL REGISTRAR required at above Hospital. Preference will be given to applicants having experience in medical emergencies. Post vacant 1st December, 1956. Hospital may be visited by direct appointment.

Application forms obtainable from Secretary, Luton and Hitchin Group Hospital Management Committee, St. Mary's Hospital, Luton. Beds, and returnable by 16th October, 1956.

HULL A GROUP HOSPITAL MANAGEMENT COM-MITTEE. SENIOR HOUSE OFFICER required in the E.N.T. Departments of the Victoria Hospital for Sick Children, and the Hull Royal Infirmary. This post is recognised for the F.R.C.S. and D.L.O.

Applications, with testimonials, should be sent to the Hospital Secretary, Victoria Hospital for Sick Children, Park-street, Hull.

HULL. KINGSTON GENERAL HOSPITAL. (419 Beds.) HULL A GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of RESIDENT JUNIOR HOUSE SURGEON (pre- or post-registration). Recognised for the F.R.C.S. examinations. Busy acute General Surgical Unit. Vacant 1st October.

Applications, with 2 recent testimonials, to the Hospital Secretary.

IPSWICH GROUP CHEST HOSPITALS. Senior House OFFICER for duties in the above Hospitals. Suitable for a doctor reading for higher qualifications with special interest in chest complaints. Will be required to reside alternately at Foxhall Hospital, Ipswich (102 Beds) for investigation and treatment of all chest diseases, where duties in the Major Surgical Unit will be involved, and Nayland (British Legion) Hospital, near Colchester (124 Beds for tuberculous and non-tuberculous pulmonary disease). Furnished quarters available.

Further details from Dr. G. R. MCNAB, Physician-Superintendent, Foxhall Hospital, Ipswich, to whom applications, with recent testimonials, should be sent.

ISLEWORTH, MIDDLESEX. WEST MIDDLESEX HOSPITAL. NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. SENIOR REGISTRAR (E.N.T. Department) required at above Hospital. Whole-time, non-resident. Hospital may be visited by direct appointment.

Application forms obtainable from, and returnable to, Group Secretary, South West Middlesex Hospital Management Committee, West Middlesex Hospital, Isleworth, Middlesex, by 23rd October, 1956.

ISLEWORTH. WEST MIDDLESEX HOSPITAL. Senior HOUSE OFFICER required for Psychiatric Unit. Duties mainly in observation wards. Post recognised by Conjoint and R.M.P.A. as D.P.M. training post.

Applications, stating age, nationality, qualifications, and experience, with copies of up to 3 recent testimonials, to Group Secretary, South West Middlesex Hospital Management Committee, West Middlesex Hospital, Isleworth, by 17th October.

KETTERING GENERAL HOSPITAL, Kettering. (170 Beds.) Applications are invited from registered medical practitioners for the appointment of SENIOR HOUSE OFFICER in Anæsthetics. Post recognised for D.A.

Applications, giving details of qualifications and experience, and enclosing copies of 3 recent testimonials, to be sent to the Group Secretary, Kettering and District Hospital Management Committee, at the above address.

LEEDS REGIONAL HOSPITAL BOARD. Registrar vacancies.

Anæsthetics

Bradford A and B Groups, preferably resident. Recognised for the F.F.A.R.C.S. Approximately 700 Beds in the surgical specialties. Establishment 1 Senior Registrar and 2 Registrars.

Chest Diseases

Leeds Chest Clinic and additional duties, as required at Regional Sanatoria. Previous experience in diseases of the chest desirable. Accommodation for a single person only at Killingbeck Hospital.

General Surgery

(*a*) Hull Royal Infirmary (80 general surgical beds) and other hospitals in the Hull A Group. Non-resident. Includes additional duties in the Casualty Department.

(*b*) Halifax Group. 1 of 3 similar posts. Duties divided approximately between general and orthopædic surgery (195 general surgical and 85 orthopædic beds). May include some duties in the Casualty Department. Preferably resident.

(*c*) Harrogate and District General Hospital (65 general surgical beds). Preferably resident. Recognised for F.R.C.S.

Orthopædic Surgery

St. James's Hospital, Leeds (64 orthopædic beds) and the Public Dispensary, Leeds. Non-resident.

Psychiatry

Scalebor Park Hospital (300 Beds). Annual admission-rate 350–400. Accommodation available for single person. Facilities for attendance at Leeds University will be provided if the successful candidate is studying for the D.P.M.

Applications, stating age, qualifications, and details of present and previous appointments with dates, together with the names and addresses of 3 referees, to the Secretary, Joint Registrars Committee, Park-parade, Harrogate, by 12th October, 1956.

LEEDS REGIONAL HOSPITAL BOARD. Short-term LOCUM TENENS appointments in the Registrar grade are constantly available at hospitals in the area of the Board, particularly in the specialties of anæsthetics, general medicine, general and orthopædic surgery, and psychiatry.

Interested practitioners, suitably experienced, should communicate with the Secretary, Joint Registrars Committee, Park-parade, Harrogate.

LEEDS REGIONAL HOSPITAL BOARD (in association with the Leeds Medical School) invites applications from fully Registered Practitioners for admission to the Regional Pathological Training Scheme. The scheme involves 4 years training, 2 as Senior House Officer and 2 as Registrar, and subject to satisfactory progress, the appointments are renewed annually.

Applications, stating age, qualifications, and details of present and previous appointments with dates, together with the names and addresses of 3 referees, should be forwarded to the Secretary, Park-parade, Harrogate, by not later than 19th October, from whom further details may be obtained on request.

LEEDS. UNITED LEEDS HOSPITALS. General INFIRMARY AT LEEDS. REGISTRAR in Psychiatry required. Non-resident post with opportunities for further training in psychiatry. Work carried out in conjunction with the University Professorial Department of Psychiatry.

Applications, stating age, qualifications and present and previous appointments with dates, with names of 3 referees, should be sent to the Sub-Dean, School of Medicine, Leeds, 2, not later than 16th October, 1956.

LEEDS. THE UNITED LEEDS HOSPITALS. The GENERAL INFIRMARY AT LEEDS. RESIDENT RADIOTHERAPY OFFICER (Senior House Officer status). The appointment is for a period of 6 months in the first instance, commencing 1st November, 1956. The post affords facilities for training for D.M.R.T. Conditions of service for hospital medical staff apply.

Applications, stating age, qualifications, previous posts with dates, and 3 names for reference, should be sent to the Secretary to the Board as soon as possible.

LANARKSHIRE AREA OBSTETRICAL AND GYNÆCOLOGICAL STAFF. Applications are invited for a post as JUNIOR HOSPITAL MEDICAL OFFICER on the above staff based at Bellshill Maternity Hospital. The work will be confined to neonatal sick infants, but applicants should have had some experience in obstetrics and gynæcology. Salary £775–£50–£1075 p.a.

Applications in writing, stating age, qualifications and giving details of experience, together with the names of 3 referees, should be lodged not later than 14 days from the date of publication of this advertisement with the Group Secretary, Board of Management, Hairmyres Hospital, East Kilbride, Lanarkshire.

LUTON, BEDFORDSHIRE. ST. MARY'S HOSPITAL. SENIOR HOUSE OFFICER (resident) required 17th October, 1956. (129 Beds mainly for Chronic Sick and 33 Beds for Chest Diseases.)

Applications, stating age, nationality, qualifications, and experience, together with copies of 3 recent testimonials, to be sent to the Secretary, Luton and Hitchin Hospital Management Committee, St. Mary's Hospital, Luton, as soon as possible.

MANCHESTER. MONSALL HOSPITAL, Newton Heath, MANCHESTER, 10. RESIDENT SENIOR HOUSE OFFICER required for infectious diseases hospital, which is a Regional Centre for Poliomyelitis. There are also 150 Beds for the treatment of tuberculosis and other chest diseases.

Applications, with names of 2 referees, to Deputy Group Secretary, Monsall Hospital, from whom further particulars may be obtained.

MANCHESTER. UNITED MANCHESTER HOSPITALS. MANCHESTER ROYAL EYE HOSPITAL. Applications are invited for the following posts :—

SENIOR HOUSE OFFICER.

HOUSE OFFICER (pre-registration surgical post).

Application forms may be obtained from the undersigned.

H. R. NORTH, General Superintendent.

Manchester Royal Eye Hospital.

MANCHESTER. UNITED MANCHESTER HOSPITALS. SAINT MARY'S HOSPITALS, MANCHESTER. Applications are invited for the post of SENIOR HOUSE OFFICER in Obstetrics, vacant 1st January, 1957. Applicants must have had previous hospital experience in general medicine and surgery, and in obstetrics. The post is recognised for the purpose of the M.R.C.O.G. examination. The duties involve clinical responsibility for mothers and babies and supervision of the work of pre-registration House Officers is also included. The appointment is for 12 months. Nat onal scale.

Application forms may be obtained from the undersigned and returned not later than 15th October, 1956.

A. R. WISE, General Superintendent.

Saint Mary's Hospitals, Whitworth Park, Manchester, 13.

MANCHESTER. WEST MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. PARK HOSPITAL, DAVYHULME. Applications are invited from suitably qualified and experienced Male or Female candidates for RESIDENT SURGICAL REGISTRAR (Thoracic Unit). This Hospital is a General Hospital of 433 Beds. It carries out by far the major part of the Manchester Region's cardiac and non-tuberculous thoracic surgery, in addition to all other major specialties. The total number of resident medical staff is 20. The successful candidate will be expected to work with each of the 3 Consultant Thoracic Surgeons attached to this unit of 50 Beds (including 10 children's beds).

Application forms from the Secretary.

MANCHESTER. WEST MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. PARK HOSPITAL, DAVYHULME. (General Hospital—433 Beds.) HOUSE PHYSICIAN (pædiatrics) required for mid-November. Post-registration. There is a Midwifery Unit of 73 Beds and a Pædiatric Unit which includes 10 thoracic surgical beds. Recognised for D.C.H.

Application forms from Secretary.

MANCHESTER. WEST MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. PARK HOSPITAL, DAVYHULME. (General Hospital—433 Beds.) SENIOR HOUSE OFFICER (non-tuberculous Thoracic Surgery) required for Manchester Regional Hospital Board Centre. Post now vacant.

Application forms from Secretary.

MANCHESTER REGIONAL HOSPITAL BOARD invite applications for the post of Whole-time REGISTRAR in General Medicine to the West Manchester Hospital Management Committee, primarily for duty at Park Hospital, Davyhulme, but with duties at other Group Hospitals. Post vacant mid-November. 12 months appointment in first instance.

Forms from Secretary, Park Hospital, Davyhulme.

MANCHESTER REGIONAL HOSPITAL BOARD. Royal MANCHESTER CHILDREN'S HOSPITAL, SALFORD HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of RESIDENT SURGICAL OFFICER (Registrar grade), falling vacant 21st November, 1956. Previous experience in surgery essential. The Hospital is the chief teaching unit of the University Department of Child Health and the post gives ample opportunity for experience in all branches of surgery in children.

Applications, stating age, nationality and experience, together with names of 2 referees, to be forwarded to the Group Secretary, Salford Royal Hospital, Chapel-street, Salford, 3, to be received not later than 20th October, 1956.

MANCHESTER REGIONAL HOSPITAL BOARD. SALFORD HOSPITAL MANAGEMENT COMMITTEE. Applications invited for the following posts :—

RESIDENT REGISTRAR in Orthopædic Surgery in the above Group, main duties at Hope Hospital.

NON-RESIDENT REGISTRAR in E.N.T. Surgery to the Salford and West Manchester Groups of hospitals, with main duties at Salford Royal and Park Hospitals.

Applications, together with names and addresses of 2 referees, to be sent to the Group Secretary, Salford Royal Hospital, Salford, 3, before 13th October, 1956.

MANCHESTER REGIONAL HOSPITAL BOARD invite applications for the post of Whole-time RESIDENT SURGICAL REGISTRAR to the West Manchester Hospital Management Committee, with duties primarily at Park Hospital, Davyhulme, but with duties at other hospitals within the Group. Post now vacant. 12 months appointment subject to renewal.

Forms from Secretary, Park Hospital, Davyhulme.

MANCHESTER, 4. ANCOATS HOSPITAL. Applications are invited for the post of CASUALTY OFFICER (Senior House Officer). Recognised for F.R.C.S. Vacant 16th November, 1956.

Applications, with names of 2 referees, by 15th October, 1956, to Group Secretary, North Manchester Hospital Management Committee, Crumpsall Hospital, Manchester, 8.

MANCHESTER (near). ASTLEY HOSPITAL. (146 Beds.) SENIOR HOUSE PHYSICIAN, vacant 16th November, for general hospital with acute medical beds, a geriatric unit and infectious disease cases. Outpatient work at Leigh Infirmary. Applicants studying for higher qualifications preferred.

Full details to Secretary, Wigan and Leigh Hospital Management Committee, Knowsley House, Wigan.

MAIDENHEAD HOSPITAL, St. Luke's-road, Maidenhead. Applications are invited for the post of CLINICAL ASSISTANT in Ophthalmology, involving 1 half-day per week on a Tuesday morning. Recent experience in ophthalmology desirable. Salary £175 p.a. per weekly half-day.

Application forms obtainable from, and returnable to, Group Secretary, Windsor Group Hospital Management Committee, Alma-road, Windsor, by 19th October.

MANSFIELD AND DISTRICT GENERAL HOSPITAL. (Recognised for training for F.R.C.S.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time RESIDENT SURGICAL REGISTRAR required. Married accommodation available. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 15th October, 1956, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

MIDDLESBROUGH. POOLE HOSPITAL, Nunthorpe, MIDDLESBROUGH. (Tuberculosis—308 Beds.) Applications are invited for the appointment of RESIDENT MEDICAL OFFICER (married accommodation available) for general duties on medical and surgical wards (adults and children). The grading and salary of the appointment will be either that of Junior Hospital Medical Officer or Senior House Officer according to the experience of the candidate and will be subject in all respects to the National Conditions of Service. This Hospital is a most modern one with an active Thoracic Surgery Unit.

Applications, stating age, nationality, qualifications, and previous experience, and the names of 3 referees, to be sent immediately to the Group Secretary, Cleveland Hospital Management Committee, West Lane Hospital, Middlesbrough.

MUSSELBURGH, MIDLOTHIAN. EDENHALL HOSPITAL. (221 Beds.) Applications are invited for the immediate appointment of SENIOR HOUSE OFFICER (general surgical).

Applications, stating age, experience, and copies of recent testimonials, to the Medical Superintendent.

NEWCASTLE GENERAL HOSPITAL. (838 Beds.) NEWCASTLE UPON TYNE HOSPITAL MANAGEMENT COMMITTEE. ANÆSTHETIST (Junior Hospital Medical Officer grade). Salary £775–£1075. The Hospital is the Regional Centre for Neurosurgery, Radiotherapy, Urology, and Cardiology, &c. Married accommodation (furnished flat) available.

Applications, with full particulars and names of 2 referees, should be sent to the Secretary, Newcastle General Hospital, Newcastle upon Tyne, 4.

NEWCASTLE REGIONAL HOSPITAL BOARD. Special AREA OF CUMBERLAND AND NORTH WESTMORLAND. REGISTRAR in Ophthalmology. Main duties at the Cumberland Infirmary, Carlisle, also duties at the Dumfries and Galloway Royal Infirmary. Single accommodation at Cumberland Infirmary.

Applications, with names of up to 3 referees, to Senior Administrative Medical Officer, 72, Warwick-road, Carlisle, within 14 days.

NEWTON ABBOT HOSPITAL. (General Section—65 Beds.) RESIDENT SENIOR HOUSE SURGEON (Male or Female) required early December, 1956. Married quarters available.

Applications (quoting ref. F.364/37), stating qualifications, nationality, age, with copy testimonials, to be sent to the Group Secretary, Torquay District Hospital Management Committee, Torbay Hospital, Torquay, S. Devon.

NORTHWOOD, MIDDLESEX. MOUNT VERNON HOSPITAL AND RADIUM INSTITUTE. NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. REGISTRAR required for Department of Pathology at above Hospital.

Application forms obtainable from, and returnable to, the Group Secretary, Harefield and Northwood Group Hospital Management Committee, Mount Vernon Hospital, Northwood, Middlesex, by 12th October, 1956.

NOTTINGHAM AND MIDLAND EYE INFIRMARY. Required SENIOR HOUSE OFFICER, duties to commence on 1st November, 1956. Salary and conditions of service in accordance with Ministry regulations. A furnished flat is available for married candidates, if required.

Applications, stating age, qualifications, and experience, together with copies of testimonials, to be sent to the Group Secretary, General Hospital, Nottingham.

NOTTINGHAM CHILDREN'S HOSPITAL. (136 Beds. Recognised for the D.C.H.) Applications are invited for the post of SENIOR HOUSE OFFICER (surgical). The post is tenable for 6 months or a year by agreement.

Applications, with copies of 2 testimonials, should be sent to the Secretary, Nottingham Children's Hospital, Chestnut-grove, Nottingham.

NOTTINGHAM. CITY HOSPITAL. (811 Beds.) Applications are invited for the post of HOUSE SURGEON, vacant 15th November, 1956. Recognised for pre-registration purposes.

Applications, stating age, nationality, qualifications and experience, together with copies of not more than 3 testimonials, to be sent to the Hospital Secretary, City Hospital, Hucknall-road, Nottingham.

NOTTINGHAM GENERAL HOSPITAL. Applications are invited from registered medical practitioners for the post of SENIOR HOUSE OFFICER (casualty) duties to commence immediately. Establishment 3. Recognised for F.R.C.S. Post offers wide experience of casualty work.

Applications, stating age, nationality, qualifications and experience, together with copies of testimonials, to be sent to the Secretary, General Hospital, Nottingham.

OXFORD REGIONAL HOSPITAL BOARD. Registrar in Thoracic Surgery at Peppard Chest Hospital, near Reading (236 Beds, including 60 for surgical cases). The special Surgical Unit contains 34 Beds. Married or single accommodation available. Post available from 1st October, 1956, for an initial period of 1 year.

Application forms obtainable from the Secretary, Registrar Committee, 43, Banbury-road, Oxford, should reach him by 22nd October, 1956.

OXFORD REGIONAL HOSPITAL BOARD: UNIVERSITY OF OXFORD. LITTLEMORE HOSPITAL, OXFORD. Applications are invited for the post of SENIOR REGISTRAR in Psychiatry at above Hospital. The successful candidate (who should hold the D.P.M. or its equivalent) may be asked to spend part of the tenure at other mental hospitals in the Region. There are facilities for postgraduate study, University teaching, and psychiatric outpatient work. Further information may be obtained from the Physician-Superintendent.

Applications, on forms obtainable from the Secretary, Oxford Regional Hospital Board, 43, Banbury-road, Oxford, must reach him by 20th October, 1956.

PLYMOUTH. SOUTH DEVON AND EAST CORNWALL HOSPITAL.

SENIOR HOUSE OFFICER in Surgery, vacant 15th November, 1956. Recognised for the F.R.C.S. Devonport Section.

HOUSE SURGEON (pre-registration post), vacant 1st January, 1957. Recognised for the F.R.C.S. Freedom Fields Section.

HOUSE PHYSICIANS (pre-registration posts), vacancies 1st and 17th January, 1957. Greenbank Road Section.

HOUSE SURGEONS (pre-registration posts), vacancies 1st December, 1956, 10th and 18th January, 1957. Recognised for the F.R.C.S. Greenbank Road Section.

Applications, stating age, nationality, qualifications and experience, together with the names and addresses of 3 referees, to be sent to—

ARTHUR R. CASH, Group Secretary, Plymouth,
South Devon and East Cornwall General Hospital Group.
7, Nelson-gardens, Stoke, Plymouth.

PLYMOUTH. THE SCOTT ISOLATION HOSPITAL. PLYMOUTH SPECIAL HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of SENIOR HOUSE OFFICER from Male registered medical practitioners who have preferably been qualified for 1 year, and have had previous hospital experience. The applicant should be able to drive a car. The duties, in 2 departments, will be chiefly in connection with infectious and venereal diseases, the former including a substantial proportion of cases in children. The varied clinical work, including acute medical cases and early pulmonary tuberculosis, provides valuable experience, particularly to those reading for a higher medical degree, or contemplating General Practice. The appointment will be for 1 year and there is an immediate vacancy.

Applications, together with copies of 2 recent testimonials, should be sent to the Group Secretary, Plymouth Special Hospital Management Committee, 8, Nelson-gardens, Stoke, Plymouth.

PONTEFRACT AND CASTLEFORD HOSPITAL MANAGEMENT COMMITTEE. JUNIOR HOSPITAL MEDICAL OFFICER to assist Geriatric Physician in the staffing of an active Geriatric Unit at hospitals in this and Wakefield A Hospital Management Committee area. Married accommodation available. Car essential.

Applications immediately to the Secretary, Great Northern House, Salter-row, Pontefract, Yorkshire.

PORTSMOUTH GROUP HOSPITAL MANAGEMENT COMMITTEE.

Royal Portsmouth Hospital

SENIOR HOUSE SURGEON. Recognised for the F.R.C.S. Vacant now.

Applications, stating age, experience, and qualifications, together with names of 2 referees, should be forwarded as soon as possible to E. H. HURST.

St. Mary's Hospital, Milton-road, Portsmouth.

PRESTON (near), LANCASHIRE. WHITTINGHAM HOSPITAL. JUNIOR HOSPITAL MEDICAL OFFICER. Applications are invited for this post at the largest Mental Hospital in the country where all modern treatment is undertaken, including electro-encephalography for the area. Facilities will be given for study either for the D.P.M. at Manchester University or for the M.R.C.P. at a large General Hospital a few miles away. The Hospital is well situated in a country district with easy access to Preston, Blackpool and Southport. Comfortable furnished quarters with full residential emoluments are available at a charge of £170 p.a. or alternatively a furnished or unfurnished flat can be arranged for a married man.

Applications endorsed "Medical Officer," giving details of experience and names and addresses of 3 referees, to be addressed to the Medical Superintendent, Whittingham Hospital, near Preston, and be received as soon as possible.

READING AREA HOSPITALS. Applications are invited for the post of SENIOR HOUSE OFFICER (pathology). Previous experience in pathology desirable, but not essential. Salary £745, less £150 board-residence.

Apply, stating age, qualifications with dates, nationality, present post, together with the names of 3 referees, to Group Secretary, 3, Craven-road, Reading.

READING. BATTLE HOSPITAL. (391 Beds.) Applications are invited from registered medical practitioners for the post of RESIDENT JUNIOR HOUSE SURGEON in the Area Accident and Orthopædic Department. Post now vacant F.R.C.S. recognised. Also casualty duties. Salary £425–£525 p.a., less £125 board-residence.

Apply, stating age, qualifications with dates, nationality, present post, with 1 copy of recent testimonial, to Hospital Secretary.

REDHILL. EAST SURREY HOSPITAL, Shrewsbury-road, REDHILL. RESIDENT HOUSE SURGEON (pre-registration appointment).

Apply Hospital Secretary, naming 2 referees.

ROMFORD, ESSEX. RUSH GREEN HOSPITAL. (301 Beds.) SENIOR HOUSE OFFICER (Male or Female) required from 14th November, 1956. Duties include work in general medicine and in the Regional Poliomyelitis Unit (30 Beds), where excellent experience of modern methods can be obtained. Resident post.

Applications to Medical Superintendent.

ROMFORD, ESSEX. VICTORIA HOSPITAL. (99 Beds.) RESIDENT HOUSE PHYSICIAN (Male) required immediately. Post not approved for pre-registration purposes.

Applications should be forwarded to the Secretary, Romford Group Hospital Management Committee, Oldchurch Hospital, Romford.

SCARBOROUGH HOSPITAL. (General—190 Beds.) Applications are invited for the post of NON-RESIDENT CASUALTY OFFICER (Junior Hospital Medical Officer) to commence duty approximately 1st November, 1956. Terms and conditions of service in accordance with those prescribed for medical and dental staffs. A furnished cottage is available for the successful applicant in the grounds of Cross Lane Hospital (1 mile distant), for which the present rent is £7 19s. 9d. per month.

Applications, giving age, qualifications, details of present and previous appointments, and the names of 2 referees, should be forwarded to the Hospital Secretary.

SCUNTHORPE, LINCOLNSHIRE. WAR MEMORIAL HOSPITAL. (262 Beds.) Vacancy for HOUSE PHYSICIAN (1 of 2) pre-registration or Senior House Officer according to experience. Busy department with medicine, pædiatrics, skins and eyes with busy outpatient clinics offering good experience.

Applications, naming 2 referees, to Group Secretary, Scunthorpe Hospital Management Committee.

SCOTTISH NATIONAL BLOOD TRANSFUSION ASSOCIATION. ASSISTANT MEDICAL OFFICER. Applications are invited for this post in the Western Regional Blood Transfusion Service with headquarters in Glasgow. In addition to the collection of blood from donors the post offers excellent laboratory experience in blood group serology. Salary £775–£1075 p.a. National Health Service (Scotland) superannuation regulations.

Apply in writing to Regional Director, Blood Transfusion Service, 15, North Portland-street, Glasgow, C.1.

SCOTLAND. SOUTH-EASTERN REGIONAL HOSPITAL BOARD. Applications are invited for the appointment of REGISTRAR in the Regional Thoracic Surgery Unit based on the Eastern General Hospital, Edinburgh, vacant on 1st January, 1957.

Applications, giving particulars of age, qualifications and previous experience, together with the names of 2 referees, should be submitted to the Secretary, South-Eastern Regional Hospital Board, Scotland, 11, Drumsheugh-gardens, Edinburgh, 3, by 27th October, 1956.

SCOTLAND. SOUTH-EASTERN REGIONAL HOSPITAL BOARD. Applications are invited for the appointment of SENIOR REGISTRAR to the Regional Plastic Surgery Service. The duties will be mainly at Bangour General Hospital, Broxburn, West Lothian, and the Royal Hospital for Sick Children in Edinburgh, and there will be outpatient work at the Royal Infirmary of Edinburgh.

Applications, giving particulars of age, qualifications, and previous experience, together with the names of 3 referees, should be sent to the Secretary, South-Eastern Regional Hospital Board, Scotland, 11, Drumsheugh-gardens, Edinburgh, 3, by 3rd November.

SCOTLAND. WESTERN REGIONAL HOSPITAL BOARD. Applications are invited for the following appointments, which will be for 1 year in the first instance :—

REGISTRAR in Surgery based at Broadstone Hospital, Port Glasgow.
REGISTRAR in E.N.T. Surgery based at the Royal Infirmary, Glasgow, for duties at Law Hospital, Carluke.
REGISTRAR in Psychiatry based at Hawkhead Mental Hospital, Glasgow.
REGISTRAR in Psychiatry based at Riccartsbar Mental Hospital, Paisley.
SENIOR REGISTRAR in Radiotherapy based at the Western Infirmary, Glasgow.
REGISTRAR in Radiodiagnosis based at the Victoria Infirmary, Glasgow.

These appointments are subject to the National Health Service (Scotland) superannuation regulations.

Applications (12 copies), stating date of birth, qualifications, experience, present appointment, and the names of 3 referees, to reach the Secretary, Western Regional Hospital Board, 64, West Regent-street, Glasgow, C.2, by 20th October, 1956.

SCOTLAND. EASTERN REGIONAL HOSPITAL BOARD. Chest Medicine and Tuberculosis. DUNDEE AREA. Applications are invited for the post of SENIOR REGISTRAR in Chest Medicine and Tuberculosis in the Dundee Area. Duties will be mainly at Ashludie Chest Hospital, Monifieth, near Dundee (222 Beds, including the Regional Thoracic Surgical Centre with 60 Beds), and the Chest Clinic in Dundee. Higher medical qualification desirable. Salary and conditions of service in accordance with national agreement.

Further particulars and forms of application from the Secretary to the Board, "Bracknowe," 430, Blackness-road, Dundee, with whom applications must be lodged not later than 27th October, 1956.

SCOTLAND. EASTERN REGIONAL HOSPITAL BOARD. Mental Deficiency. BALDOVAN INSTITUTION. Applications are invited for the post of SENIOR REGISTRAR at Baldovan (Mental Deficiency) Institution by Dundee. The present bed complement of 400 Beds is being developed to 750. It is a centre for a system of clinics for the mentally handicapped at Dundee, Perth, Arbroath and Montrose set up in operation with the Local Authorities. The Institution is associated with the Medical School in Dundee for purposes of undergraduate and postgraduate teaching. Salary and conditions of service in accordance with national agreement.

Forms of application and further particulars from the Secretary to the Board, 430, Blackness-road, Dundee, with whom applications must be lodged not later than 27th October, 1956.

SHEFFIELD. CITY GENERAL HOSPITAL. (Recognised for Final Fellowship examination.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time RESIDENT or NON-RESIDENT SURGICAL REGISTRAR required at the above Hospital. The successful candidate to reside at the Hospital when "on call." This is a large general hospital with teaching affiliations. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 15th October, 1956, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time SENIOR REGISTRAR in Psychiatry required for Middlewood Hospital, Sheffield (2098 Beds). A flat (2 bedrooms) is available. D.P.M. essential. Appointment for 1 year in the first instance, reviewable annually. Opportunity for research and experience in the special branches of psychiatry available in the Hospital area.

Application forms and further details obtained from Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield. Forms to be returned by 15th October, 1956.

SHEFFIELD. THE UNITED SHEFFIELD HOSPITALS. Applications invited for the following posts:—

(*a*) NON-RESIDENT REGISTRAR in General Surgery, with duties in the Urological Department at the Royal Hospital. Post vacant 13th December, 1956.

Closing date for applications 13th October, 1956.

(*b*) REGISTRAR in Thoracic Surgery at the Royal Infirmary. Post vacant 15th December, 1956.

Closing date for applications 20th October, 1956.

Applications, with the names of 3 referees, should be sent to the Chief Administrative Officer, The United Sheffield Hospitals, West-street, Sheffield, 1.

SHOREHAM-BY-SEA, SUSSEX. SOUTHLANDS HOSPITAL. (411 Beds.) Applications are invited for the post of OBSTETRIC AND GYNÆCOLOGICAL REGISTRAR (55 Beds). M.R.C.O.G. preferred. The post will be vacant from 1st January, 1957.

Forms of application can be obtained from the undersigned, and must be returned as soon as possible.

A. V. OAKTON, Group Secretary,
Worthing Group Hospital Management Committee.
129, Brighton-road, Worthing, Sussex.

SHREWSBURY. ROYAL SALOP INFIRMARY. (216 Beds.) HOUSE SURGEON, vacant 1st November, 1956. Pre-registration candidates eligible. Recognised for the F.R.C.S.

Applications, with copy testimonials, to Group Secretary, Shrewsbury Hospital Group, Royal Salop Infirmary, Shrewsbury.

SHREWSBURY. ROYAL SALOP INFIRMARY. ORTHOPÆDIC ACCIDENT HOUSE SURGEON (Senior House Officer). Successful applicant will be allowed to attend for 2 days a month at the Robert Jones and Agnes Hunt Orthopædic Hospital, Oswestry, for postgraduate study, with the Consultant. Post recognised under revised Fellowship regulations in respect of 6 months training required for the Final Fellowship examination. Vacant 1st November, 1956.

Applications, with copy testimonials, to Group Secretary, Shrewsbury Hospital Group, Royal Salop Infirmary, Shrewsbury.

SHREWSBURY. ROYAL SALOP INFIRMARY AND COPTHORNE HOSPITAL. (500 Beds.) GYNÆCOLOGICAL HOUSE SURGEON. 50 gynæcological beds and 2 House Surgeons. Post recognised for M.R.C.O.G. Vacant 20th November, 1956.

Applications, with copy testimonials, to Group Secretary, Shrewsbury Hospital Group, Royal Salop Infirmary, Shrewsbury.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for the appointment of REGISTRAR in Dental Surgery to the Tunbridge Wells Group of hospitals. The duties will be mainly carried out in the Special Jaw Centre of the Plastic and Maxillo Facial Unit at East Grinstead. A higher dental qualification is desirable. The appointment will be in accordance with the terms and conditions of service of hospital medical and dental staffs (England and Wales), and will be for 1 year in the first instance.

Applications, giving particulars of age, qualifications, and experience with relevant dates, together with the names and addresses of 2 referees, to be sent to the Secretary, Registrars Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, London, W.1, not later than 27th October, 1956.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for an appointment as Whole-time REGISTRAR in Ophthalmology to fill a vacancy in the approved trainee establishment at the Brighton and Lewes Group of hospitals, for duties mainly at the Sussex Eye Hospital, Eastern-road, Brighton, 7. The post is recognised for the F.R.C.S. and D.O. and may be either resident or non-resident; no accommodation is available for a married practitioner. The appointment will be in accordance with the terms and conditions of service of hospital medical and dental staffs (England and Wales), and will be for 1 year in the first instance.

Applications, giving particulars of age, qualifications, and experience with relevant dates, together with the names and addresses of 2 referees, to be sent to the Secretary, Registrars Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, W.1, not later than 20th October, 1956.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. CANTERBURY, ISLE OF THANET, AND SOUTH EAST KENT GROUPS OF HOSPITALS. Applications are invited for 2 appointments as REGISTRAR in Orthopædic Surgery, 1 to the Canterbury and Isle of Thanet Groups and the other to the Canterbury and South East Kent Groups; duties will rotate annually between the 2 appointments, which offer experience in traumatic work and in general orthopædic surgery, including long-stay cases. The appointments will be in accordance with the terms and conditions of hospital medical and dental staffs (England and Wales).

Applications, giving particulars of age, qualifications, and experience with relevant dates, together with the names and addresses of 2 referees, to be sent to the Secretary, Registrars Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, London, W.1, not later than 20th October, 1956.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. ST. FRANCIS AND HURSTWOOD PARK HOSPITALS, HAYWARDS HEATH, SUSSEX. 2 PSYCHIATRIC REGISTRARS required at above Mental Hospital and Neuropsychiatric Unit. In addition to the neurological and psychiatric facilities of these hospitals, trainees may attend the practice of the Mental Health Department in Brighton, the Brighton Observation Ward, and the Brighton Child Guidance and Adult Outpatient Clinics. Married and single accommodation available. The appointments will be in accordance with the terms and conditions of service of hospital medical and dental staffs (England and Wales) and will be for 1 year in the first instance.

Applications, giving particulars of age, qualifications, and experience with relevant dates, together with the names and addresses of 2 referees, to be sent to the Secretary, Registrars Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, W.1, not later than 20th October, 1956.

SOUTH ELMSALL. WARDE-ALDAM HOSPITAL. Applications are invited for the post of RESIDENT SURGICAL OFFICER (Senior House Officer grade). Warde-Aldam Hospital is a general hospital of 39 Beds (general and orthopædic surgery and E.N.T.). Furnished flat available. Duties mainly in Casualty Department.

Applications, giving details of qualifications and previous experience, with names of 2 referees, to be forwarded to the undersigned as soon as possible.

D. G. DAVIES, Group Secretary.
Great Northern House, Salter-row, Pontefract, Yorks.

SOUTHAMPTON. ROYAL SOUTH HANTS HOSPITAL. (278 Beds.) ORTHOPÆDIC HOUSE SURGEON required. Post recognised for Pre-registration Service and tenable for 6 months. The Hospital is the centre to which all trauma from a large industrial town and port is directed thus providing excellent experience in the treatment of traumatic conditions; patients with orthopædic conditions are also drawn from a wide area.

Applications, with copies of testimonials, should be sent as soon as possible to the Group Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SOUTHAMPTON. ROYAL SOUTH HANTS HOSPITAL (274 Beds) and SOUTHAMPTON GENERAL HOSPITAL (472 Beds). SENIOR HOUSE OFFICER (E.N.T.) required beginning of October. This post is recognised for the F.R.C.S. (Eng.) and D.L.O. examinations and provides experience in all branches of E.N.T. work. The Group includes a diagnostic and distributing Hearing Aid Centre.

Applications, with copies of recent testimonials, should be forwarded as soon as possible, to the Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SOUTH CHESHIRE HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER (anæsthetics). Male or Female. 6 months or 12 months as preferred. Approved for D.A. Duties chiefly at general hospital and Maternity Unit. Previous experience is not essential. Salary and conditions as per regulations.

Applications, stating age, details of experience, qualifications and names of 3 referees, immediately to Group Secretary, Barony Hospital, Nantwich.

SOUTHEND GENERAL HOSPITAL. Applications are invited for the post of SECOND CASUALTY OFFICER (Senior House Officer grade) with duties in the Fracture and Orthopædic Department. Resident. Post vacant 22nd October, 1956. The post is recognised for F.R.C.S.

Applications, stating age, qualifications and experience, with copies of recent testimonials, to reach the undersigned by 10th October, 1956. J. C. FIELD, Secretary.

STOKE-ON-TRENT. NORTH STAFFORDSHIRE ROYAL INFIRMARY. HOUSE OFFICER (general surgery) required. Pre-registration post. Hospital recognised for F.R.C.S.

Detailed applications, with copy testimonials, to Group Secretary, Hospital Management Committee, Princes-road, Stoke-on-Trent.

STOKE-ON-TRENT. NORTH STAFFORDSHIRE ROYAL INFIRMARY. HOUSE OFFICER (orthopædics) required. Recognised pre-registration post. Hospital recognised for F.R.C.S.

Applications, with copy testimonials, to Group Secretary, Hospital Management Committee, Princes-road, Stoke-on-Trent.

ST. ALBANS CITY HOSPITAL, St. Albans, Hertfordshire. (384 Beds.) HOUSE PHYSICIAN (House Officer grade) required for 1 of the 2 medical teams for duties mainly on the acute wards. Post vacant 8th November and tenable for 6 months. Preference given to candidates seeking post under the Medical Act, 1950.

Applications to Secretary, Mid-Herts Group Hospital Management Committee, Bleak House, Catherine-street, St. Albans.

ST. ALBANS CITY HOSPITAL, St. Albans, Hertfordshire. (384 Beds.) HOUSE SURGEON (House Officer grade) required for general surgical team. Recognised for F.R.C.S. Post vacant 2nd November and tenable for 6 months. Preference given to candidates seeking post under the Medical Act, 1950.

Applications to Secretary, Mid-Herts Group Hospital Management Committee, Bleak House, Catherine-street, St. Albans.

SULLY HOSPITAL, Sully, Glamorganshire. Senior HOUSE OFFICER (surgical) required as soon as possible at above Hospital. (Regional Thoracic Centre, 324 Beds.) Experience gained in investigation and treatment of all chest and heart conditions.

Form of application from Group Secretary, Cardiff Hospital Management Committee, 44, Cathedral-road, Cardiff.

SWANSEA HOSPITAL, Swansea. (403 Beds.) Glantawe HOSPITAL MANAGEMENT COMMITTEE. Registered medical practitioners are invited to apply for the locum appointment of RESIDENT ANÆSTHETIST (Senior House Officer grade), at the above Hospital. The Hospital is recognised under the D.A. and F.F.A.R.C.S. regulations.

Applications, stating age, qualifications and experience, together with copies of 2 recent testimonials, should be forwarded to the Hospital Secretary. T. E. JONES, Group Secretary.

TUNBRIDGE WELLS (near). PEMBURY HOSPITAL, PEMBURY. Applications invited for post of HOUSE PHYSICIAN (Senior House Officer) in Paediatric Unit. Previous pædiatric experience desirable. Post vacant 1st December, tenable for 12 months and recognised for D.C.H. examination.

Apply, stating age, qualifications and experience, with 3 recent testimonials, to Group Secretary, Sherwood Park, Pembury-road, Tunbridge Wells.

WARRINGTON GENERAL HOSPITAL. (344 Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER (pædiatrics), Male or Female, which will become vacant on 1st December, 1956. Post recognised for D.C.H. Scale of salary £745 p.a., less £150 for residential emoluments.

Applications to be forwarded to—

H. L. BOOT, Group Secretary,

Warrington and District Hospital Management Committee, c/o General Hospital, Warrington, Lancs.

WELSH REGIONAL HOSPITAL BOARD.

REGISTRAR in Orthopædic Surgery to serve Cardiff Hospital Management Committee. Based at Prince of Wales Orthopædic Hospital, Rhydlafar, near Cardiff (200–300 Beds). Hospital is Regional Orthopædic Centre for South Wales area. Married accommodation available.

REGISTRAR in Psychiatry, Whitchurch Hospital, Cardiff (800 Beds). Single accommodation available.

REGISTRAR (obstetrics and gynæcology). Based Royal Gwent Hospital, Newport, Mon (260 Beds), to attend neighbouring hospitals. Accommodation for a lady doctor available at County Hospital, Griffithstown.

Subject to review end of first year.

Application forms from Senior Administrative Medical Officer, Temple of Peace, Cathays Park, Cardiff, within 14 days.

WIGAN (near). WRIGHTINGTON HOSPITAL. Junior HOSPITAL MEDICAL OFFICER required (resident or non-resident). Manchester Regional Centre for orthopædic tuberculosis. 200 adults and 100 children. Salary £775–£50–£1075 p.a.

Apply to Secretary with 2 references.

WIGAN (near). WRIGHTINGTON HOSPITAL. Senior HOUSE OFFICER required (resident or non-resident). Regional Centre for orthopædic tuberculosis. 200 adults and 100 children. Salary £745 p.a.

Apply to Secretary with 2 references.

WOLVERHAMPTON. NEW CROSS HOSPITAL. (627 Beds.)

Pre-registration HOUSE OFFICER in Medicine, vacant 15th October.

Pre-registration HOUSE OFFICER in General Surgery, vacant 31st October.

Applications to Hospital Secretary.

WAKEFIELD. PINDERFIELDS GENERAL HOSPITAL. Applications invited for position of SENIOR HOUSE OFFICER in the Thoracic Surgery Department. Salary £745 p.a. A charge of £150 p.a. is made for accommodation.

Address written applications, giving full personal particulars and details of experience, &c., together with 2 names and addresses for reference, to W. BOWRING, Group Secretary.

Victoria Chambers, Wood-street, Wakefield.

WAKEFIELD. PINDERFIELDS GENERAL HOSPITAL. Applications invited for appointment of JUNIOR HOSPITAL MEDICAL OFFICER for the Leeds Regional Thoracic Centre (59 Beds) at Pinderfields General Hospital. The Centre deals with thoracic and upper abdominal surgery in association with the Thoracic Consultants of the General Infirmary at Leeds. Salary scale £775–£50–£1075 p.a., less a charge of £170 for board, lodging, &c. Married accommodation available.

Address written applications, with full particulars and 2 names and addresses for reference, to—

W. BOWRING, Group Secretary.

Victoria Chambers, Wood-street, Wakefield.

WAKEFIELD. STANLEY ROYD HOSPITAL. Applications invited for post of JUNIOR HOSPITAL MEDICAL OFFICER in Psychiatry. Salary scale £775–£50–£1075. Married accommodation may be available.

Address written applications, giving full personal particulars, details of training, experience, &c., together with 2 names and addresses for reference, to W. BOWRING, Group Secretary.

Victoria Chambers, Wood-street, Wakefield.

B.W.I. UNIVERSITY COLLEGE HOSPITAL OF THE WEST INDIES. Applications are invited for the posts of REGISTRAR or SENIOR REGISTRAR in Medicine and in Pædiatrics in this teaching hospital, approved by the London University for its degrees. The successful candidates will be required to commence duties by 1st January and 14th February, 1957, respectively. The appointments are for 1 year in the first instance. Salary is payable within the scale £900–£100–£1100/£1200–£100–£1500 p.a., depending on experience and qualifications. Single accommodation and board are provided at a deduction of £145 p.a. Sea passage will be provided.

Further information may be obtained from the Hospital Manager and Secretary, University College Hospital of the West Indies, Mona, Jamaica, B.W.I., to whom applications stating age, nationality, qualifications, and experience, together with names and addresses of 3 referees, should be sent by 10th November, 1956.

CANADA. OTTAWA GENERAL HOSPITAL. Applications for appointments to the RESIDENT STAFF for the year commencing 1st July, 1957, are now being received. This is a 600-Bed teaching general hospital affiliated with the Medical School of Ottawa University. Postgraduate training in medicine, obstetrics, and gynæcology, pædiatrics, pathology, psychiatry, and surgery is approved by The Royal College of Physicians and Surgeons of Canada towards the fellowship or specialty certification and for junior rotating internship by the Canadian Medical Association. Remuneration from $900 to $1800 p.a. Travelling expenses advanced to selected candidates from overseas.

Apply to Medical Director, Ottawa General Hospital, 43, Bruyere-street, Ottawa 2, Ontario, Canada.

ST. JOHN'S, NEWFOUNDLAND, CANADA. GENERAL HOSPITAL. (475 Beds.) The above Hospital has several vacancies for INTERNES for which applications are invited. Salary is $2500 p.a., less $480 for maintenance. There is a full teaching programme. The Hospital is fully approved by the Canadian Medical Association for Intern Training and also approved by the Royal College of Physicians and Surgeons in Canada for Postgraduate Training towards Certification. Transport to St. John's, Newfoundland, will be paid, and on completion of 1 years service, return fare to the United Kingdom will be provided.

Applications, with full details as to age, &c., together with names of 2 referees, should be forwarded immediately to—

Dr. E. WILSON, Superintendent.

General Hospital, St. John's, Newfoundland, Canada.

Public Appointments

COVENTRY CORPORATION HEALTH DEPARTMENT require immediately Temporary ASSISTANT MEDICAL OFFICER for approximately 3 months. Combined maternity and child welfare/school health work. Salary £1050 p.a.

Apply Medical Officer of Health, New Council Offices, Coventry, within 1 week.

DERBYSHIRE COUNTY COUNCIL. Appointment of ASSISTANT COUNTY MEDICAL OFFICER OF HEALTH for the Derbyshire County Council and MEDICAL OFFICER OF HEALTH for the Borough of Ilkeston and the urban districts of Alfreton, Heanor and Ripley. Applications are invited from Male or Female registered medical practitioners holding a Diploma in Public Health or an equivalent qualification for the above-named permanent "mixed" appointment. The total inclusive salary scale will be £1936 2s. 9d. p.a.–£57 0s. 11d. (3)–£58 15s. 0d. (1)–£55 2s. 3d. (1)–£18 15s. 0d. (3)–£2277 7s. 9d. p.a. A car allowance is payable. The person appointed will be directly responsible to the Councils of the Borough of Ilkeston and the Urban Districts of Alfreton, Heanor and Ripley for the proper performance of all the duties of a Medical Officer of Health for those areas respectively. As Assistant County Medical Officer he will be concerned under the direction of the County Medical Officer of Health with decentralised supervision required under the National Health Service, as well as work in connection with the School Health Service, attendance at clinics, and such other duties as may be required. The person appointed may be required to reside in the area of the District Councils. Sympathetic consideration will be given to the provision of housing accommodation if required. The officer must not engage in private practice, and must devote the whole time to the duties of the before-mentioned posts. The appointment is subject to the provisions of the Local Government Superannuation Acts, 1937/53. The successful candidate will be required to pass a medical examination. Canvassing, either directly or indirectly, will be a disqualification.

Application forms may be obtained from the undersigned, to whom they should be returned so that they are received not later than 15th October, 1956.

J. B. S. MORGAN, County Medical Officer of Health.

County Offices, Derby.

MANCHESTER EDUCATION COMMITTEE. Medical OFFICERS are required for work in the School Health Service. Salary £1050–£1475. Preference given to candidates with experience in children's diseases and retinoscopy and holding D.P.H. or D.C.H.

Application forms and particulars (stamped addressed envelope) from Chief Education Officer, P.O. Box 480, Manchester, 3, returnable to the Town Clerk, Town Hall, Manchester, 2, by 27th October, 1956. Envelope to be endorsed School Medical Officer.

MANCHESTER CORPORATION HEALTH DEPARTMENT. ASSISTANT MEDICAL OFFICER required for duties mainly concerned with the City Council's schemes for immunisation and vaccination. Salary £1050–£50–£1200–£55–£1475. Medical Council "C" conditions of service.

Application forms (returnable by 13th October, 1956) from the Town Clerk, Town Hall, Manchester, 2.

TREASURY MEDICAL SERVICE. Applications are invited from medical practitioners, practising in the districts detailed below, for appointment, in a part-time and mainly advisory capacity, as LOCAL TREASURY MEDICAL OFFICER for each of the places or groups of places shown. The town shown in brackets after the place-names indicates the Head Post Office Area in which the place, or group of places, is situated. Successful applicants will be required to examine and report on the condition of certain Government Officers, teachers, candidates for appointment, &c., who may be referred to them from time to time; and to attend when summoned to an emergency case of accident or sudden illness occurring in a Government office in the neighbourhood. Fees for this work, and mileage allowance where necessary, will be paid on a scale agreed with the British Medical Association.

Intending applicants should write, within 14 days, to Treasury Medical Adviser, Treasury Chambers, Whitehall, S.W.1, for a form on which application may be made. Applicants should be not more than 60 years of age.

The places for which applications are invited are as follows :—

ENGLAND AND WALES

Broadclyst (Exeter). Bramley (Guildford).
Totton (Southampton).

SCOTLAND

Kilmarnock (Kilmarnock). Bellshill (Motherwell).

NORTHERN IRELAND

Florencecourt and Letterbreen (Enniskillen).

YORKSHIRE. DIVISIONAL ADMINISTRATION OF THE PREVENTIVE MEDICAL SERVICE IN THE ADMINISTRATIVE COUNTY OF THE WEST RIDING OF YORKSHIRE. Appointment of MEDICAL OFFICER OF HEALTH AND DIVISIONAL MEDICAL OFFICER to Cudworth, Darfield, Darton, Dodworth, Royston, Wombwell, and Worsbrough Urban District Councils and the County Council of the West Riding of Yorkshire. Applications are invited from registered medical practitioners who must also be registered in the Medical Register as the holder of a Diploma in Sanitary Science, Public Health, or State Medicine, for the above-mentioned whole-time appointment. The effect of the "mixed" appointment will be to secure that the planning of the day-to-day administration and the execution of all or practically all public health matters of the division will be in the hands of 1 person, the Divisional Medical Officer of Health. A Divisional Public Health Office with necessary staff will be provided.

The salary attached to the post is as follows :—

(a) For Medical Officer of Health duties: £975–£27 10s. 0d. (4)–£25 (1)–£1110 0s. 0d.

(b) For County Council duties: £981 5s. 0d.–£31 5s. 0d. (1)–£34 7s. 6d. (7)–£1253 2s. 6d.

(The salary scales have been calculated in accordance with the recent award to Public Health Medical Officers.) In addition, there will be a travelling and subsistence allowance at the rate of £180 p.a.

The appointment will be made jointly by the District Councils and the County Council and the person appointed will not be permitted to engage in private practice.

Forms of application and terms and conditions of service may be obtained from the County Medical Officer, County Hall, Wakefield, to whom completed forms must be returned not later than 24th October, 1956. Canvassing of members of the appointing bodies directly or indirectly will disqualify any candidate for the post.

F. POTTER, Clerk of the Wombwell Urban District Council.
J. WOOD-WILSON, County Medical Officer.

STATE PUBLIC SERVICE
QUEENSLAND, AUSTRALIA

MEDICAL OFFICERS (Mental Hygiene Service)

Applications are invited from qualified Medical Practitioners for appointment as Medical Officers at the Brisbane Mental Hospital and the Ipswich Mental Hospital, Department of Health and Home Affairs, with salary-range minimum £A2071 10s. p.a., maximum £A2251 10s. p.a., inclusive of present basic wage adjustments and subject to any further such adjustments. Salary in excess of the minimum may be paid according to the qualifications and experience of each appointee.

Applicants must be registrable as Medical Practitioners in Queensland. An extra £A100 p.a. in addition to normal salary is payable if the appointees are qualified for registration as Psychiatrists in Queensland. The appointees may be required to conduct sessions at the Psychiatric Clinics in Brisbane and Ipswich respectively.

Appointment includes provision of free quarters, fuel, light, milk and garden produce or an allowance in lieu of same.

Further particulars may be obtained from the Agent-General for Queensland, 409 and 410 Strand, London, W.C.2.

Applications should contain particulars of full name, date of birth, marital status, children (if any) and any war service, and full details of qualifications and experience, and should be accompanied by references or certified copies of references.

Applications should be forwarded by air-mail so as to reach the Secretary, Public Service Commissioner's Department, Box 488H, G.P.O., Brisbane, Australia, by 12th November, 1956.

SURREY COUNTY COUNCIL. Wimbledon Borough COUNCIL. Applications invited for the mixed appointment of COUNTY DIVISIONAL (part) AND BOROUGH MEDICAL OFFICER OF HEALTH. Salary £1968 p.a., rising by annual increments to £2355 p.a. Commencing salary according to experience. Appointment subject to medical examination and to Local Government superannuation acts.

Applications, stating age, qualifications, and experience, with names of 3 referees, to Town Clerk, Town Hall, Wimbledon, S.W.19, by 19th October, 1956.

W. W. RUFF, Clerk of Surrey County Council.
FRANCIS J. O'DOWD, Town Clerk of Wimbledon.

General Practice

For an Executive Council post (England and Wales) apply on form E.C.16A obtainable from the council. Mark envelope "Vacancy."

COUNTY BOROUGH OF HUDDERSFIELD. Executive COUNCIL. Applications are invited for VACANCY (death) in Lindley area (urban). List approximately 2800. Residence and surgery available. Apply on Form E.C.16A to the undersigned before 17th October, 1956.

H. HOLLAND,
Huddersfield Executive Council.

49, New North-road, Huddersfield.

COUNTY BOROUGH OF READING EXECUTIVE COUNCIL. Applications are invited from registered medical practitioners for a VACANCY on a new Corporation housing estate of approximately 1100 houses, shops, &c. Residence and surgery on estate provided by Corporation. (Rent and rates £158 p.a., rising to £294 p.a. after May next—negotiations proceeding for possible reduction.) Present doctor taking up appointment overseas. National Health Service list approximately 950. Applications on Form E.C.16A should reach the undersigned not later than 20th October next. Further particulars available on request.

J. BLUNDEN, Clerk of the Council.

10, Gun-street, Reading, Berks.

Medical Ophthalmic practice (supplementary and private) for sale. Locum required immediately. Death vacancy. Leeds. —Apply: Address, No. 247, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

Hospital Services : Non-Medical Appointments

U.S.A. LACONIA HOSPITAL, Laconia, New Hampshire, U.S.A. There is a vacancy for a TECHNICIAN with special experience in biochemistry. Laconia is a summer and winter resort in the lake district of New England.

For particulars apply to the Pathologist.

Miscellaneous

Evans Medical Supplies Ltd. invite applications from Male, registered medical practitioners, having specialised knowledge in bacteriology, for the post of Bacteriologist at The Evans Biological Institute, Runcorn, Cheshire. This senior position should appeal to Medical Bacteriologists who are technically interested in the research into and the manufacture of immunological products for therapeutic purposes. The terms and conditions of service will not be inferior to those which maintain in the National Health Service.

Applications, giving full particulars of age, qualifications, and experience, should be forwarded to The Medical Director, THE EVANS BIOLOGICAL INSTITUTE, Runcorn, Cheshire.

Winnipeg, Manitoba, Canada. Applications are invited for the post of Prediatrician, in the Winnipeg Clinic. Specialist qualifications are required. Work is with a group of Specialists actively engaged in private practice. Starting salary minimum $6000 p.a., plus other benefits including pension.

Applications, stating age, qualifications, experience, 2 references, should be sent to The Director, Winnipeg Clinic, Winnipeg.

Clerical Assistant, Male or Female, good shorthand-typist, required in small professional office in City of London. —State age, experience, and salary required to: Address, No. 249, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

Secretary, highly experienced medical work, seeks part-time employment.—Ring: WELbeck 3833.

Surgeon wishes to dispose of consulting-room mahogany desk, 4′ 6″ by 2′ 6″ by 2′ 6″, flat-top in leather, knee-hole, drawers on either side, high-class construction and in excellent condition, £27. Instrument cabinet on stand, £10. Also many instruments for gynæcological and general surgery if required. View London on application.—Address, No. 248, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

For Sale. 1 G.E.C. battery-operated Electro-cardiograph Model B number 117614. 1 Cambridge portable Electro-cardiograph, mains/battery operated. Instrument No. 136889/C145734. (Not including stand or battery.)

Offers to be made to the Secretary, Birkenhead Hospital Management Committee, St. James Hospital, Tollemache-road, Birkenhead.

"Pregnancy Diagnosis by the Xenopus Method," 24-hour service. Send specimen of urine and £1 1s. fee. Haematology, Biochemistry, Flame Photometry.—WELBECK BIOLOGICAL LABORATORIES, 26, Park-crescent, Portland-place, W.1 (MUSeum 5386–7).

Applicants for posts requiring testimonials copied or duplicated should communicate with MANTON SECRETARIAL SERVICE LTD., 98, Victoria-street, S.W.1 (Phone: VICtoria 0141), who are specialists in this kind of work.

Professional, technical and personal typewriting. Dupli-cating, circularising, &c., efficiently and speedily executed.—"MOWBRAY," 146, Bishopsgate, E.C.2 (BIS. 2545, BAR. 7665).

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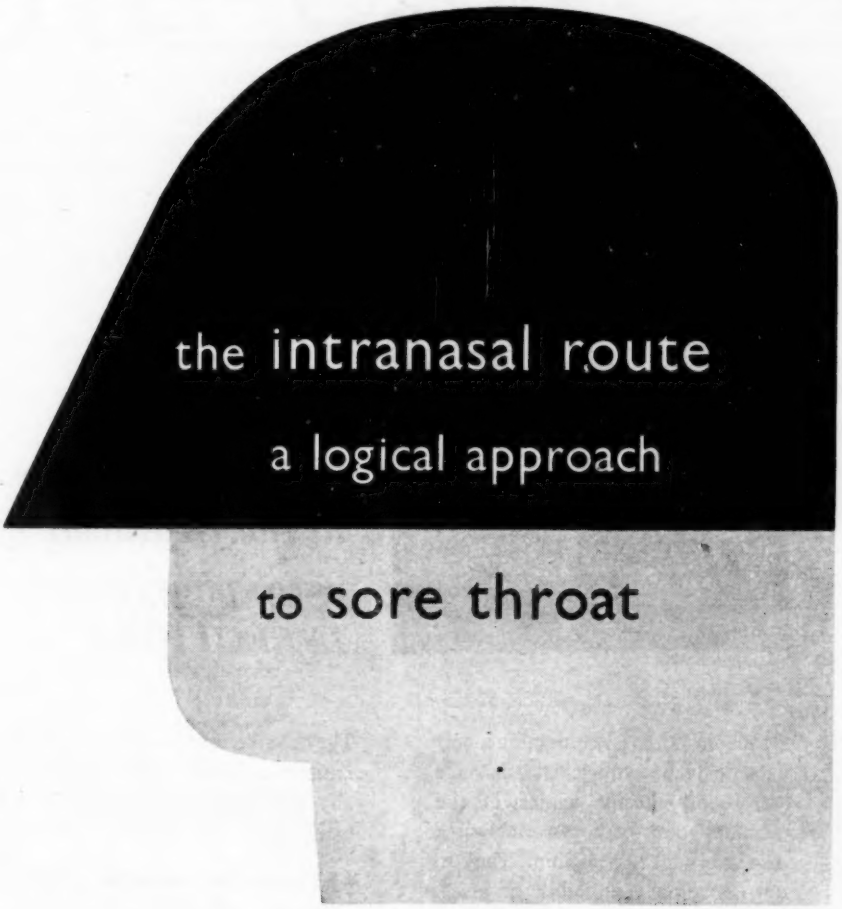

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Part of the suspension drifts down over the nasopharynx and pharynx, producing potent, long-lasting bacteriostasis just where it is needed most—at the site of infection in the throat.

Sulfex a *suspension* of microcrystalline sulphathiazole highly effective in sore throat

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